THE American Journal OF Gastroenterology

VOL. 22, NO. 1 JULY, 1954

Panel Discussion on Latest Developments in Cancer of the Gastrointestinal Tract

Clinical Studies of Blood Lipid Metabolism

Nonparasitic Cyst of the Spleen

The Surgical Management of Congenital Megacolon

Clinical X-ray Staff Conferences on the Colon

Diarrheal Syndrome

Favorable Clinical Results in Cardiospasm with Anticholinergic Medication

Nineteenth Annual Convention
Washington, D. C.
25, 26, 27 October 1954

Official Publication
NATIONAL GASTROENTEROLOGICAL ASSOCIATION

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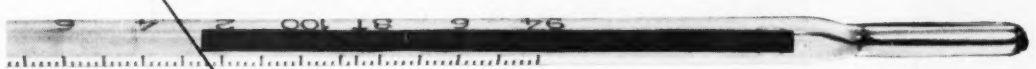
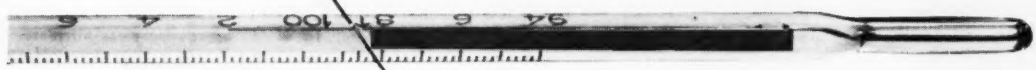


and time is a factor...



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1. Flippin, H. F.: Philadelphia Med. *49*:733 (Jan. 30) 1954.
2. Glatt, M., and Ross, S.: Antibiotics & Chemotherapy *4*:395 (Apr.) 1954.

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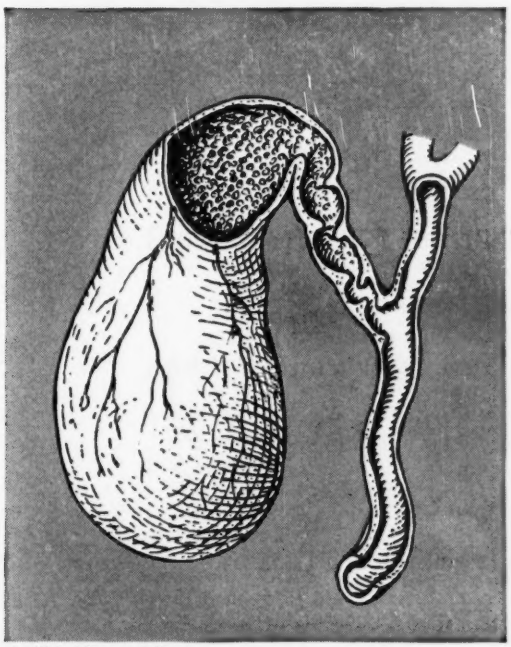

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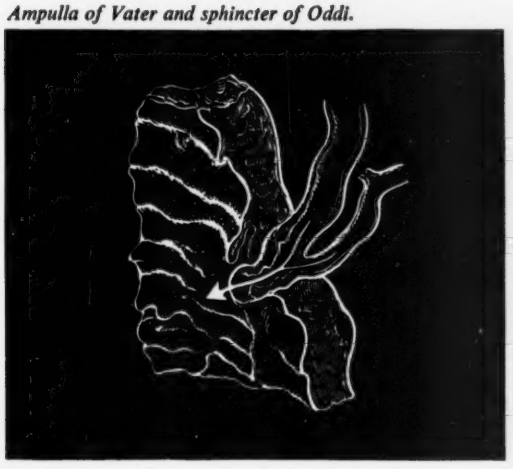
1. Berg, A. M., and Hamilton, J. E.: A Method to Improve Roentgen Diagnosis of Biliary Diseases with Bile Acids, Surgery *32*:948 (Dec.) 1952.

Ampulla of Vater and sphincter of Oddi.



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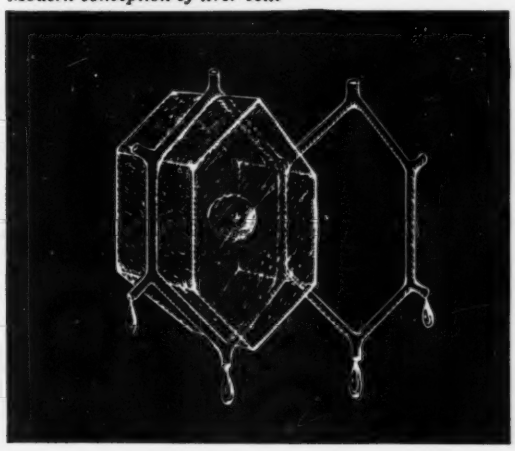

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(FORMERLY THE REVIEW OF GASTROENTEROLOGY)

The Pioneer Journal of Gastroenterology, Proctology and Allied Subjects in the United States and Canada

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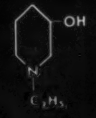

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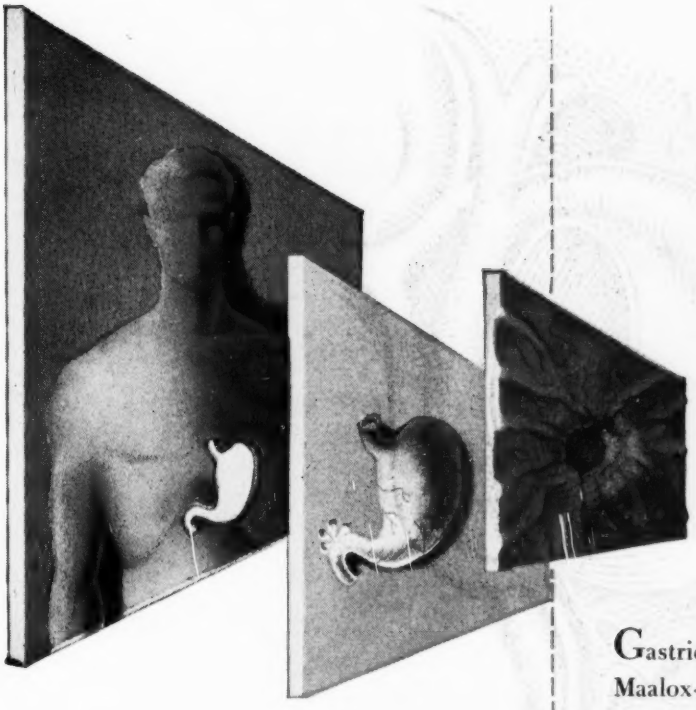

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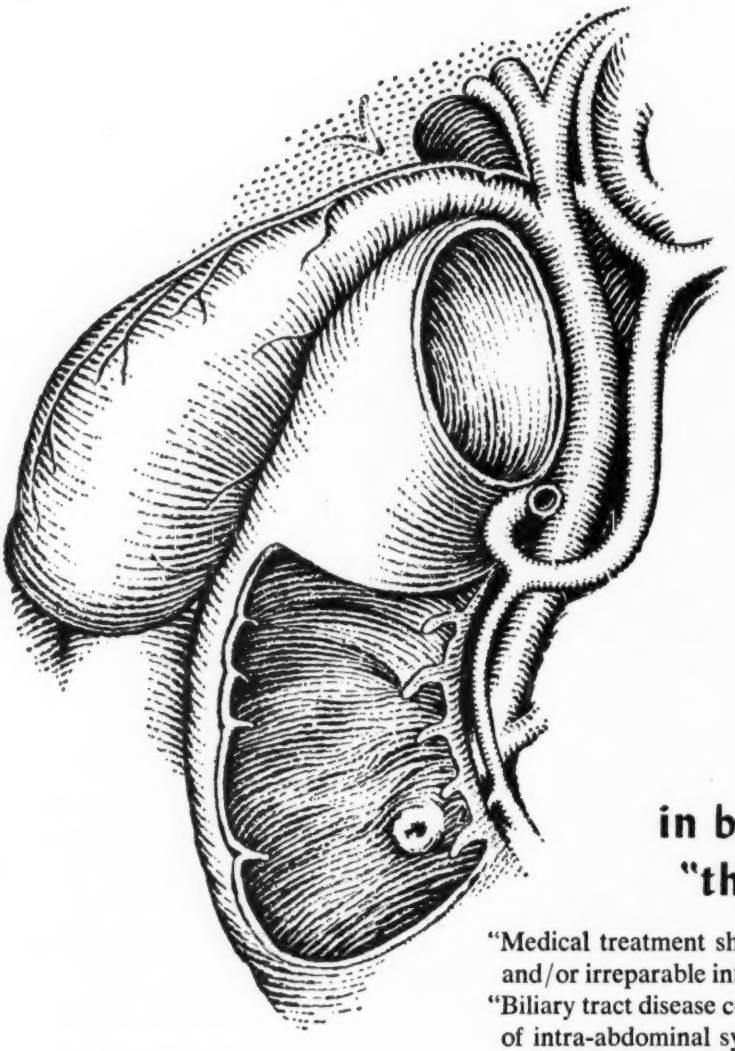

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1. Segal, H.: Postgrad. Med. *13*:81, 1953. 2. O'Brien, G. F., and Schweitzer, I. L.: M. Clin. North America *37*:155, 1953. 3. Beckman, H.: Pharmacology in Clinical Practice, Philadelphia, W. B. Saunders Company, 1952, p. 361.

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THE American Journal OF Gastroenterology

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VOLUME 22 JULY, 1954 NUMBER 1

PANEL DISCUSSION ON LATEST DEVELOPMENTS IN CANCER OF THE GASTROINTESTINAL TRACT*

WILLIAM C. BOECK, M.D.
WILBUR BAILEY, M.D.
JAMES A. HALSTED, M.D.
Los Angeles, Calif.
and
OWEN H. WANGENSTEEN, M.D.
Minneapolis, Minn.

Dr. Boeck:—I am not used to this at all, being an amateur, and I hope you will bear with me. The subject this afternoon for panel discussion is a very long one. It covers I think about twenty feet of gastrointestinal tract, from the top to the bottom. Sometimes the middle of the roast is often the best part, and we may confine most of our discussions to the middle of this gastrointestinal tract.

In discussing the latest developments in the treatment of the cancer or diagnosis of cancer of the gastrointestinal tract, it doesn't always mean that the latest developments mean something new. I say that because I think we are sort of crystalizing a great deal of our knowledge in arriving to some extent at a consensus among medical men as well as among surgeons and certainly in the roentgen diagnosis of lesions, so that there is a greater unanimity of procedure. So, today, some of the things that you may hear from members of the Panel, may not necessarily mean as I say, discoveries, but what is now more or less the accepted procedure or the method of diagnosis.

It gives me great pleasure to introduce to my left, Dr. Wangensteen of the University of Minnesota. You all know him I am sure.

At his left is Dr. Bailey, a roentgenologist here in Los Angeles. He is also somewhat of a politico, being our Past President of the Los Angeles County Medical Society at one time. They do get outside of their field once in a while.

*Presented before the Eighteenth Annual Convention of the National Gastroenterological Association, Los Angeles, Calif., 12, 13, 14 October 1953.

At his left is Dr. Halsted from the Veterans Administration. Dr. Halsted is head of the Gastroenterology Department at Wadsworth Hospital.

I thought we could skip over all the lesions so far as the oral cavity is concerned, and start with a discussion of cancer of the esophagus, and the most important thing perhaps is to know when you do have a cancer of the esophagus. I'd like to have Dr. Halsted tell us when we ought to suspect that a patient might have a cancer of the esophagus and what measures he would take to find out whether he did have one.

Dr. Halsted:—Any patient who complains of difficulty in swallowing, that is, dysphagia, should be suspected of having cancer of the esophagus. The first thing I would do would be to have an x-ray examination. If this showed any abnormality or suspicion of carcinoma I would then have an esophagoscopy performed. This should be carried out by the thoracic surgeon or endoscopist, rather than the gastroenterologist as a rule, because it is a somewhat dangerous procedure, particularly when biopsy is necessary, as it is in this situation. In fact, more than one biopsy may be necessary to make a diagnosis.

Dr. Boeck:—Thank you. Dr. Bailey, would you tell us if there are any new developments or what are the principles for the roentgen diagnosis of cancerous lesion of the esophagus?

Dr. Bailey:—Most of you know about the radiological side of carcinoma of the esophagus. I should like to have Dr. Wangensteen continue the discussion.

Dr. Wangensteen:—There is no good way to manage cancer of the esophagus. Let me put it that way to start with. Successful surgery of cancer of the esophagus is relatively new. Sauerbruch wrote several volumes on thoracic surgery, including a long tract on the esophagus, but he had no successes to report. Franz Torek, at the Lenox Hill Hospital in New York City in 1913, did an exteriorization for cancer of the esophagus, bringing the thoracic esophagus, bearing the cancer, out in the neck. The patient survived 12 years, and fed herself through a rubber tube prosthesis. That method was used by a lot of surgeons but there were very few temporary successes and no permanent cures. It remained for a Japanese surgeon, Osahwa from Kyoto, Japan, to have the first success with primary resection for cancer of the lower esophagus. Now his success has been duplicated in every area of the world. Most of the present-day operations for cancer of the esophagus were done and reported by Martin Kirschner in 1920. Martin Kirschner had no successes to report with efforts directed at removing the cancer and reestablishing continuity. Kirschner said it took him an hour and fifteen minutes to do the operation. He felt that he could succeed if he could learn to do the operation in an hour!

Those of you who have witnessed these operations for cancer of the esophagus know they are involved and concern a lot of surgery. Any job to be well done cannot be done in a hurry.

Osahwa (1933) began his article by throwing tradition to the winds and saying it took 3 or 4 hours. Most surgeons would take at least that length of time to do the operation today. I suppose the area in which there may be some competition with forms of therapy other than surgery is in the cervical esophagus. There the results are notably poor. I have the impression, however, that they are becoming better.

Richard Sweet of Boston, who is perhaps the keenest present-day exponent of surgery of cancer of the esophagus in our country, reported a mortality for excision of the lower end of the esophagus as low as 10 per cent. And the five-year survival rate was in the area of 40 per cent in patients when the lymph nodes were uninvolved. In surgery for cancer of the esophagus, surgeons must come to do radical surgery; the esophagus must not be amputated a centimeter or two above the lesion. I think virtually the greater length of the thoracic esophagus should be removed and excised for a cancer of the lower third. When surgeons come to do that generally and learn the minutiae of dealing with the many facets of the operation, I believe that this part of the alimentary canal will be dealt with just as satisfactorily as cancer of other segments of the alimentary tract. But in the neck, I think the revolving chair for radiation which Nielson in Copenhagen devised, constitutes real competition for present-day surgery in dealing with cancer of the cervical esophagus. Yet, many of us are still trying to remove these cancers of the cervical esophagus, reestablishing continuity. It may prove feasible in certain cases to do an end-on tracheostomy, excising the larynx and the cervical esophagus, migrating the colon up to be anastomosed with the pharynx. That obviously is a formidable operation. But in many cases, nothing less will suffice, if the patient is to be managed surgically.

Dr. Boeck:—Dr. Bailey, are there cancerous lesions of the esophagus that you would be willing to treat with x-ray if turned down by the surgeon?

Dr. Bailey:—Radiologists usually have cases of esophageal cancer referred to them only when the surgeons feel they are inoperable. Recently much is heard about the so-called rotational therapy. In such treatment the patient is rotated in a chair, while the x-ray beam is directed at the esophagus, usually under fluoroscopic guidance. The advantage of this type of therapy is that the esophagus gets a maximum amount of radiation, while the skin, which, of course is a limiting factor, gets a minimum amount of radiation. Since, however, multiple ports have been used for many years. It is difficult to believe that the rotational therapy will do more than slightly improve our present results. Of course, unless the beam is carefully directed—a thing which is rather difficult to do—the lesion may be missed entirely.

Dr. Russell Morgan of Baltimore, who has been interested in intensifying the image on the fluoroscopic screen for many years, now is perfecting a device by means of which a receptor may be placed behind the patient. This instrument will then transmit an image to a television screen located on the control

panel. Should the patient slump down in the chair, and many of them do, various remotely controlled motor-driven devices are available to move him back to the proper position. Needless to say, radiologists welcomed Dr. Morgan's announcement, for we have long hoped to be able to get fluoroscopic results in a dimly-lighted room rather than having to do so much of our work in rooms about as dark as a coal mine.

Dr. Boeck:—Thank you, Dr. Bailey. Well, I think that covers the esophagus fairly well and we will turn now to the next organ and that is the stomach. Again, diagnosis of cancer of the stomach is a most important thing that has to be done first, and I think we rely first upon the x-ray department for the diagnosis. I would like to ask Dr. Bailey again if there are any new developments or new signs or technics that the roentgenologists now employ to be a little more certain of what their diagosis is.

Dr. Bailey:—We are considerably concerned about some of the publicity that goes with cancer detection centers and also the so-called minifilm, or small film, examinations of the stomach. Many of us feel that the cancer detection center should really be the office of the doctor who first sees the patient for, generally speaking, detection centers have proven over the years simply to be places where a physical examination is done with special emphasis on detection of cancer. Any good doctor, of course, will do the same thing in his own office. Unfortunately, in order to keep some of these "detection centers" crowded with patients, radio advertising has been used which has resulted in an undesirable atmosphere of commercialism.

All of us have, of course, been interested in Dr. Morgan and his minifilm examinations of the stomachs of some 10,000 people. Naturally, radiologists are skeptical of any examination for cancer of the stomach in which films alone are used, for we have found that even when we do our best with fluoroscopy and everything else, we sometimes miss the smaller lesions. As I understand it, in the first 10,000 minifilm examinations of the stomach, some seven cases of cancer were discovered. One was operated upon immediately, but the other patients wished to wait until they had symptoms. It would appear, therefore, that although this technic is interesting, it will scarcely be possible to x-ray every individual's stomach every year. Moreover, there is always the danger, of course, that a patient will be given a false sense of security because he thinks he had had a complete x-ray examination. It would seem that a good many early lesions might go through such a crude sieve as the minifilm examination.

Since the general consensus seems to be that the cancer detection centers have shown, after a fair trial over the years, to be of no great advantage, I should like to have Dr. Wangensteen comment on how we might shrink the 20-month delay period which he believes usually occurs between the time the cancer starts and the patient finally comes to the doctor.

Dr. Wangensteen:—Well, to err is a pretty human frailty. No one makes perfect diagnosis routinely, and I think Dr. Bailey is quite right in suggesting that now and then we convey to a patient a sense of security upon which he has no just claim, merely because he has been examined. Certain it is that in cancer detection centers, in clinics and in the offices of physicians, lesions are overlooked occasionally.

I think in any encounter the first thing to do is to knock that arch enemy, pride, off his stool; if one will do that, one can begin to resolve the other issues on the level at which they may be dealt with.

I would say this: until we have biologic tests for cancer, we must continue to send asymptomatic patients, who may have cancer (patients of our age group), to cancer detection centers where the examiners are cancer minded. At the University of Minnesota, Dr. David State, now of Los Angeles, inaugurated our cancer detection center. Until reliable organ scrutiny tests for asymptomatic cancer are found, the arduous labors of cancer detection centers, whether done in the physician's office or under special arrangements, must continue. In our cancer detection center, supported by the Minnesota Division of the American Cancer Society and sponsored by the Council of the Minnesota State Medical Society, the patient must be 45 years of age to be admitted. He must give his physician's name to whom the report is to be mailed or he will not be accepted. For cancer of the breast and cervix, and even for cancer of the colon and rectum, 45 years of age obviously is a little high to catch all cases. Yet, the age must be at that level when the incidence of cancer begins to make itself felt.

I believe the experience of our cancer detection center suggests definitely that this activity is worthwhile, particularly is this true of the great frequency with which rectal and colon polyps (precursors of cancer) are found. Moreover, in all cancers found, whether in the colon, stomach or elsewhere, a much larger number of lymph node negative cancers are found than in the hospital experience, where patients come for treatment on the basis of symptoms.

That involvement of the regional lymph nodes with cancer worsens the outlook we all know. Over the past 10 years, at the University of Minnesota however, the five-year survival rate for patients with gastric cancer in whom the lymph nodes were found uninvolved was a little better than 50 per cent. For the year 1944, the figure was 65 per cent, a figure which begins to approximate what is current surgical accomplishment for lymph node negative cancers of the rectum, colon and breast. Obviously, some of the difference is still constituted in part, by the incompleteness of the operation for gastric cancer. Gradually, however, the primary operation for gastric cancer is becoming better standardized.

Cancer of the stomach is curable. The important thing is to get over to the other side of the woodpile where the green wood is. We have been working on the dead wood—on patients with cancers that are 2 years old when the patients

first came for treatment. Some of the currently performed operations are hardly worth the extensive labor involved because in too many instances the palliation is not what the patient, the family or the physician had hoped for. We must keep ever in mind the importance of reducing not only the 6 months interval of delay after the onset of symptoms, but also the more important matter of trying to find visceral cancers during the long asymptomatic interval of 20 months, when the cancer is silent.

I heard Harrington of the Royal Cancer Society speak at the Cincinnati meeting of the American Cancer Society a year ago last year. He said, using a Churchillian phrase: "we were at the end of the beginning". If we are near the end of any beginning it is perhaps on the diagnostic side. I can well believe that within the decade which lies ahead of us some specific diagnostic agent, useful in the early detection of internal cancers, may be found. It may sound a bit heretic to say this now, but I believe that, when and if such agents come, such early cancer detection would give a more important forward thrust to the general management of the cancer problem than the discovery of the cause of cancer. Why do I say this? Where are we now in the problem of tuberculosis? It is 75 years since the tubercle bacillus was discovered; nevertheless the problem today is still the discovery of the early case. We are far enough advanced today in the knowledge of cancer to know that the problem is essentially that of early case finding. That is an important beginning. As Dr. Bailey said, gastric cancer and probably all visceral cancers are silent for about 20 months. Moreover, we know that 6 months will elapse after the first symptom before the patient finally gets his cancer diagnosed. That circumstance we lament, but let us not forget the 20 months represented by the long silent interval.

Dr. Boeck:—Another method of diagnosis that is to supplement x-ray diagnosis has been by the means of gastroscope. There are probably some of you in the audience who would like to know the opinion of the members of the Panel on the value of gastroscopic examination and the differentiation of possible malignant lesions. I have heard some surgeons say that they didn't believe it was of any help whatsoever. Some surgeons are, I am sure, quite more indulgent and go along with it to some extent. I would like first to hear Dr. Halsted from his own experience, which is very vast out at the Veterans Hospital, tell us what he thinks of the value of gastroscopic examination as a supplemental procedure in diagnosing cancer lesions of the stomach.

Dr. Halsted:—At our hospital the surgeons are very polite and indulgent but they don't really think that gastroscopy is of much value. I shall be interested to hear what Dr. Wangensteen has to say. My own feeling is that it does not have outstanding value in diagnosing gastric lesions. Let us first take the patient with a gastric lesion which, by x-ray, is either obviously malignant or there is a definite suspicion of malignancy. This patient should be operated upon at once, and gastroscopy is unnecessary. In the large group of patients with a gastric ulcer, however, in which no one can be quite sure, either from clinical or x-ray

evidence, whether it is benign, gastroscopy may be of some value. A few years ago we analyzed the gastroscopic findings in about a hundred gastric ulcers. We found that if the ulcer appeared to be what is called typically benign by gastroscopy, that is, an ulcer which is round or oval with sharp edges and a white base with little or no infiltration around it, then it proved to be benign in 95 per cent of the cases. If, however, the gastroscopy disclosed some suspicion of malignancy from the appearance of the lesion even though not obviously malignant, namely that the base might be a dirty brown color possibly with a little bleeding, and with irregular edges or some infiltration around it, that even in this situation the ulcer turned out to be benign in about 75 per cent. Here the gastroscopy helps to determine the diagnosis. When there is a definite question of the ulcer being malignant immediate surgery is indicated, and there is a small group of cases where only gastroscopy will provide this suspicion. Lastly, in the patient with a diffuse lesion by x-ray which may be gastritis or an infiltrating tumor, the biopsy gastroscope may be of value, but in our hands this instrument has not proved to be of great help because only a positive finding is conclusive. All in all I would say gastroscopy is not of outstanding value in the cancer problem. It does have a place in certain cases.

Dr. Boeck:—Dr. Wangensteen, what do you think?

Dr. Wangensteen:—I rather agree with what Dr. Halsted has said. Gastroscopy has real but limited value. A competent roentgenologist is perhaps the most important person in the recognition of a gastric cancer. In determining in a group of asymptomatic patients, which patients should be submitted to x-ray examination, we have leaned heavily on the criterion of achlorhydria or hypochlorhydria—no free HCl, or less than 30° after histamine administration. Certainly every patient should have a proctoscopic examination and every patient should have his stomach pumped. Every now and then a silent cancer is found. Any patient who has a colic polyp should have an air contrast study of the colon. Any patient with occult blood in the stool or anemia deserves a very thorough and complete study.

The accompanying slide details the story of a very interesting patient. This man, a well-known Judge in our area, was once the owner of this stomach (slide). He had been diagnosed as having a duodenal ulcer by a roentgenologist; an internist told him he had coronary disease; in consequence the patient carried nitroglycerin in his pocket and took it when he had pain. He then came, on the advice of his family physician, to see me. The first thing we did was to ascertain whether the Judge's stomach contained free HCl. He was achlorhydric. The patient was then submitted to repeated x-ray examinations of the stomach. No lesion was found despite the circumstance that our roentgenologists were informed that the patient was achlorhydric. He was then gastroscoped. A very large superficial, shallow ulcer was described by Dr. R. S. Ylvisaker, our gastroscopist. Our roentgenologist, than whom there is none better, Dr. Leo

G. Rigler, then reexamined the patient and detected evidence of a lesion which he had failed to note previously when uninstructed by the gastroscopic findings.

I explored the patient but could feel no definite lesion in the stomach. Nevertheless, I excised 95 per cent of his stomach. If I were to do it again, I would do a total excision. The Judge remains well, six years later; gastroscopy in this instance obviously was the agency which brought the patient to surgery. Yet the presence of achlorhydria was very helpful. The excised stomach exhibited the lesion which Dr. Ylvisaker had described. It was a Borrmann IV type of cancer. One lymph node was involved.

Dr. Bailey, would you offer a word in defense of the radiology?

Dr. Bailey:—I am afraid you are correct. I recently received a letter stating we had overlooked a big carcinoma of the stomach. When we reviewed the films we found to our considerable relief that the examination had actually been done by someone else. The surgeon who operated, despite the negative x-ray report, assured us that such things happened to all radiologists, however, and that even surgeons sometimes made mistakes.

So far as gastroscopy is concerned, most radiologists are disappointed, because ordinarily the same locations in which gastroscopic examination is unsatisfactory, such as the fundus of the stomach, are precisely those which are difficult to visualize by x-ray. On the subject of gastric ulcers, do you feel that nearly all should be resected, or is such a statement too radical?

Dr. Wangensteen:—Well, perhaps I should speak after Dr. Halsted on this subject, but I would say that certainly more patients should be operated upon for gastric ulcer than we are now conventionally doing. I could not, however, go so far as some of my good colleagues who would have every patient with a gastric ulcer operated upon as soon as the diagnosis is made. There is, I think, a hot-house and a garden variety of gastric ulcer; with the help of the roentgenologist, ordinarily the garden variety of gastric ulcer can be differentiated and recognized. Certainly there should be no harm in treating such a patient conservatively with a Sippy diet for 3 weeks to see if it will not heal out completely. The hot-house variety of gastric ulcer occurring in unusual locations such as the prepyloric area is more suspect than the garden variety of gastric ulcer in the usual location at the infundibulum on the lesser curvature. Such ulcers should be excised without delay. Moreover, every chronic gastric ulcer, with a persistent defect, should be operated upon. It has been said that the incidence of malignancy runs from 10 to 20 per cent in such chronic gastric ulcers, believed, prior to operation and microscopic study, to be benign.

There is one phase of this question which does not relate itself directly to the problem of malignancy but which bears nevertheless on it. Some years ago, my colleagues and I decided we would study a group of gastric ulcers—acute gastric ulcers, treating them medically. For 3 to 4 weeks, these patients

were maintained on a Sippy regimen. In addition, bed rest, beyond the hour of normal sleep was accorded some of the patients. At the expiration of this period of time, of the 13 patients in the series, complete healing appeared to have occurred in all roentgenologically. Gastric resection was carried out upon the 13 patients with their consent; one of them proved to have a cancer; of the other remaining 12, only one was completely healed microscopically. In the others, whereas epithelium came out from either side of the defect, there was still a microscopic unhealed mucosal defect in each. This circumstance, I feel, explains very clearly the nature of frequent recurrences of a gastric ulcer after apparent healing at the very same site. It never did heal completely in the first instance. There being no mucosa there, no resistance to acid-peptic digestion is present and reccurrence comes about.

Yes, I do agree we should operate on more gastric ulcers than we are currently doing, but I cannot go so far as to say that that diagnosis of a gastric ulcer is a compelling indication for immediate surgery. Now, I will be interested to hear what Dr. Halsted has to say about all this.

Dr. Halsted:—I agree in general with your point of view, Dr. Wangensteen. I think as a guess that perhaps 75 per cent of gastric ulcers should be subjected to gastrectomy. Maybe Dr. Boeck would like to discuss this. He and I have arguments about it every week out at our hospital.

Dr. Boeck:—Well, the members of the Panel have sort of jumped the gun on me. They are two pages ahead. It is rather interesting to pick up the last volume of Oxford Looseleaf Medicine on Treatment and read that 95 per cent of all the gastric ulcers will heal, and then to hear what you hear now, that we should operate on more of them. I would like some day to take a roll call of everyone here in the audience or any medical audience and ask how many of you would have your stomach operated before you gave it a four week trial at least on medical management, and very strict medical management. I don't know how many of you were at the AMA meetings in June, but there was a very important paper written and read there by members of the Lahey Clinic, who had followed 1,000 gastric ulcers for as long as from one to 22 years. Of that group, 912 were benign, 88 were malignant. That's 8.8 per cent. Of that group for example, they subjected many of their cases to surgery because they thought they might be malignant, and I think they drew a worthwhile conclusion from that study. They followed a group that was subjected to surgery because they thought they had malignancy and then compared the morbidity and symptomology of that group with another group just as large that had not been subjected to surgery, and found that they more or less had the same sort of complaints. In other words, the ones who were operated on and were cured by surgery and the others that were cured by medicine still had the same gastric complaints after they got through. They were not necessarily related to the ulcer directly. From these investigations they concluded that there is no harm in treating these patients *intensively*, and I emphasize the word, for at least four weeks to see whether

the ulcer is decreasing in size and even to follow that with gastroscopic examination before you make up your mind to subject the ulcer to surgery.

Now I think you all know Frank Lahey. Some of his papers recently and some of the members of his surgical department were on record as saying we ought to operate more of these gastric ulcers. I think it was highly significant on that day that Dr. Lahey got up and retracted all of his later publications and said, in effect, that they were due to too much enthusiasm by his own surgical fellows. That from now on, as far as the Lahey Clinic was concerned, they would be guided by this study which means they're going to treat these cases if there is any question of malignancy for at least four weeks, and if they do not show healing, they will be operated. But if they do show healing or signs of healing, they will go along further and see if they don't heal. I think that is my viewpoint and it is one I try to follow.

Dr. Wangensteen:—Four weeks, yes; but four months or longer is too long. We all put the radiologist on a very high pedestal. Some regard a competent radiologist in this field of diagnosis as being almost infallible, because he is so much more clever than we are in these differentiations. Yet every once in a while, a frank amateur like myself at the art of roentgen diagnosis will pick up a lesion that the roentgenologist himself has overlooked. My associate, Dr. Leo G. Rigler and I have been all through this; Dr. Rigler has adopted the philosophy of outlook in making his reports such that, if he has any reservations over whether the lesion may not be benign, he frankly states in the report: "the possibility of cancer cannot be excluded". Such a report has a very sobering effect on the physician responsible for the patient's care. Such a statement serves to alert you and me and everybody carrying responsibility for the patient. If every radiologist would do that, I feel certain that not nearly as many gastric cancers would be treated by medical management.

Dr. Boeck:—I think that is taken for granted, because if you are going to treat these cases intensively, they must be x-rayed once more at the end of two weeks and again at the end of four weeks. Otherwise you are not following them adequately at all. That may be a chore for some patients to do, but I think that is the essential thing that one has to do. It doesn't make any difference as to the size of the lesion. I wouldn't go longer than four weeks unless there was some evidence of the ulcer healing. But I remember a case out in the Wadsworth Hospital, and Dr. Halsted will remember this very well, a cardiac that had a couple of coronary thromboses. We were sure he would not even pull through the operation. He had achlorhydria, he had a benign ulcer as big as a dollar on the lesser curvature of the stomach. It was benign when they took it out. Interestingly enough, he pulled through this operation beautifully and nothing happened to him at all. So we said after that that we didn't think coronaries and heart diseases were any contraindication to surgery if it was really needed. I think that these cases just can't be forgotten. You will have to take them in hand and study them and treat them intensively and that doesn't mean give them

Pro-banthine and your antacids on any haphazard schedule. You have to have plenty of it. You have to know what they're doing and be satisfied. You may have to put them to bed and rest so as to get them away from business worries and what not. If things aren't favorable at least you have given them the benefit of the doubt and then go ahead with surgery. That is a fair way to look at it.

Well now here we have reached a discussion of some of the precancerous conditions. One, that we might discuss is the benign adenomas of the stomach. Dr. Wangensteen, do you take them all out?

Dr. Wangensteen:—In any program where gastric analysis is used routinely to assess patients who come for examination, some achlorhydric patients will be found. And if the achlorhydric patients are studied and followed, a number of them will be found to have gastric polyps. In our program, a large number of gastric polyps have been found. We do not do willy-nilly excision of every gastric polyp diagnosed. There does not seem to be a good reason to do a gastric resection for a pea-sized polyp. There is such a thing as the postgastrectomy syndrome; many patients suffer more from that following gastric resection than they did from the polyps. Such polyps need to be followed closely, however, for some of them do become malignant.

Gastric polyps were found in 49 out of 1,448 achlorhydric patients uncovered in a gastric cancer precursor study at our hospital. Seventeen gastric cancers were found in this same group of patients. We have patients, in whom a small gastric polyp is found, submitted to gastroscopic examinations twice a year. If the polyp exhibits growth, the patient is advised to have a gastric resection. Of the 49 polyps uncovered in the study referred to above, three on excision were found to be malignant. From our hospital records, 47 other cases of gastric polyps have been uncovered, making a total of 96 cases. My associate, Dr. Lyle J. Hay (*Surgery* **33**:446, 1953) has submitted this entire group to careful study. Of polyps more than two centimeters in diameter, Hay found 50 per cent of them to be cancerous. Among the 96 gastric polyps, seven were cancerous. If on roentgen and gastroscopic examinations, a polyp is found, an operation is advised; operation is advised also for multiple polyps. Other than that, we are content to follow these patients by periodic x-ray and gastroscopic examinations. When the polyps increase in size or number, gastric resection is advised. Gastric polyps are an occasional precursor of gastric cancer. Most of us take a more aggressive view of colic and rectal polyps, which are quicker precursors of cancer than is the gastric polyp.

Dr. Boeck:—I have just been handed a question which Dr. Wangensteen may answer regarding the value of the Papanicolaou or cytological diagnosis of malignancy of the stomach. Papanicolaou's own paper on the matter in the 1951 Journal of Cancer answers the question very well. He stated that he didn't believe it would account for more than 60 per cent of the diagnoses, or if it is going to miss 40 per cent, you don't want to use it because x-ray is much

better. The trouble with cytological diagnosis of the stomach is that you get so many foreign cells, not only from the esophagus that have to be differentiated from those of the stomach, but even swallowed, and you have a problem much more difficult than doing the cytological on bronchial specimens alone in suspected cancer of the lung.

Dr. Wangensteen:—You have had a larger experience with this technic than we. Cooper, at the New York Hospital, employs an interesting technic. He uses a balloon with a hair-net on it that engages and catches fragments of the gastric wall on it when the balloon is inflated. How well Cooper would succeed in the recognition and detection of asymptomatic gastric cancers remains to be seen. If he can do that, it will be a very important contribution.

Dr. Halsted:—I should like to emphasize that meticulous care in carrying out the technic is necessary if one is to expect to obtain reliable results. Under such conditions, however, and by using some of the technics recently described by Rubin* one may expect a high degree of accuracy. The most important essential in working with the Papanicolaou method in stomach washings is that some one doctor, who is personally interested and experienced, carry out the whole procedure. One cannot merely write an order for this as you would for a gastric analysis and expect to get any results which will be of any great value.

Dr. Boeck:—We might bring up here some other diagnostic tests or at least the value of them. There are a number of tests that have been proposed for cancer diagnosis on the basis of changes in serum proteins. Out in this city Drs. West and Penn have been doing a great deal of work on that and there are other methods as well. Dr. Wangensteen, what do you think about these methods so far as their real shortcomings?

Dr. Wangensteen:—I have no experience in diagnosing cancer of the stomach by this method. What do West and Penn do?

Dr. Boeck:—I don't know the mechanism of the tests. Dr. Halsted, do you know?

Dr. Halsted:—I don't know. A lot of it is being done out our way but they haven't talked very much about it yet. They are accumulating a great deal of information before they publish it.

Dr. Boeck:—A general critique about it was published the other day, about all these tests that too often they yield false positive or negative findings. That is going to be the trouble with any tests that is to be found. So until one is at least as accurate as x-ray is, I don't see much hope for these tests being more efficient than what we have.

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*Rubin, C. E., Massey, B. W., Kirsner, J. B., Palmer, W. L. and Stonecypher, D. D. The Clinical Value of Gastrointestinal Cytologic Diagnosis. Gastroenterology, **25**:119, 1953.

There is a method of Dr. Weinberg's, Dr. Wangensteen, of injecting the wall of the stomach with methylene blue so it diffuses into the lymphatics and stains the lymph glands. I have seen some of his sections showing cancer in the lymph glands. Is that being used very much by surgeons?

Dr. Wangensteen:—Some surgeons use pontamine sky blue and hyaluronidase to expedite diffusion of the dye to visualize the lymph node areas to which a cancer may metastasize. In any cancer operation, the important thing one must do is remove the entire *potential* lymphatic drainage area with the cancer. The surgeon must, of course, be on the lookout for lymph nodes in unconventional areas. In this regard, Dr. Weinberg's technic is helpful. We are just beginning to define the necessary magnitude of an acceptable primary operation for gastric cancer. It has to be a big operation, with removal of many areas of lymph node drainage—along the hepatic artery, the superior border of the pancreas, along the splenic artery, removing the spleen and its pedicle up to the tail of the pancreas. Any positive lymph nodes along the superior aspect of the pancreas, suggest the necessity of removing the portion of the pancreas beyond the involved lymph nodes. When surgeons do that regularly in operations for gastric cancer, the results of surgery for gastric cancer will be even much better than they are now.

My associate, Dr. Stuart Arhelger has observed, in studying recurrences in the "second look" procedure for gastric cancer, that there are two areas where recurrence is frequently observed: (1) along the superior border of the pancreas, (2) in the gastrohepatic omentum along the bile ducts. This latter area must too, therefore, be included in the lymphatic drainage area removed at the initial operation.

Dr. Boeck:—I was going to ask you in a frank case of cancer of the stomach, just how much and what you did remove. You have just answered that I think very well. We might skip on. The time is getting short.

Dr. Bailey:—One question more. I am pleased indeed at the recognition the radiologist has received, especially when he said he could take a second look and even a third one. They are entitled to have another look. You know what happens to be one of Dr. Wangensteen's hobbies too, a second look. Tell us about it.

Dr. Wangensteen:—We have had considerably more and a happier experience in the colon. Skip it until we get down there.

Dr. Boeck:—Dr. Halsted, suppose you tell us what would lead you to suspect from symptomatology and examination and other means at your disposal, that the patient might have a cancer of the colon?

Dr. Halsted:—I am sure that you are all aware of the fact that a patient who has a sudden change in bowel habits should be investigated for carcinoma

of the colon. The patient with unexplained anemia may have a carcinoma, particularly of the right colon which may bleed slowly for a long period of time resulting in profound anemia without any abdominal symptoms. The right colon and cecum are larger in diameter than other areas and the lesion has to become fairly large before it causes narrowing which would lead to cramps and pain. In addition to unexplained anemia, and change in bowel habits, gross bleeding is the other sign which must make one suspicious of carcinoma of the colon.

Dr. Boeck:—With those symptoms and signs the next thing ordinarily done, I imagine by most of us, would be rectal digital and sigmoidoscopic examinations. It is rather interesting how often that procedure is just allowed to lapse and no one thinks about doing it. That is too bad because I think everyone has a finger and should use it. After that is over with, however, we rely then upon Dr. Bailey here to tell us where the lesion is, and are there any new technics that are being used now like high voltage or air injections that will show up some of them?

Dr. Bailey:—The price of success in discovering polyps which we like to find if we can, even though they are normal or any other type of lesion is to do it and back up and do it again if you aren't sure, and then sometimes you miss. There are things such as you suggest, all sorts of new and gluey mixtures. The trouble with them is that the men who bring them to you always show them at the meeting and bring the best ones and leave the others at home. But we hope we can get some answers on something that sticks to the colon and is a little more—let's not say x-ray proof, but allows the x-ray to penetrate. One of the other ways of getting through the various stuffs we use of course is to mix them a little thinner and use 125 kilovolts instead of 70 or 80 as previously. The big trick is actually to penetrate the colon to see what is in it instead of having a wall of barium between you and the polyp. I could talk all evening on the subject of various different things to inject, but you'd rather hear from Dr. Wangensteen about what he does when we do find one.

Dr. Boeck:—Dr. Wangensteen, what would be your method of approach in surgery to lesions which are distributed in different areas of the colon.

Dr. Wangensteen:—If I may be permitted just a brief digression, I would like to say that in rectal and colic cancer there is certainly one area in which cancer detection activities in the physician's office would establish the great importance of being on the lookout for polyps and early signs of cancer. My former colleagues, Dr. David State, now of Los Angeles, and Dr. Irving Enquist, of Brooklyn, have reported (1952) that 17 per cent of asymptomatic patients over 45 years of age, visiting our cancer detection center, are found to have polyps of the rectum and the colon; most of these are found within the reach of the sigmoidoscope on proctoscopic examination. That is a surprisingly high figure. We have now known for many years (since 1940) that cancer of the colon and rectum, considered as one organ, takes more lives annually in the United States than any cancer of any other organ. Certain it is that every individual in this

audience who is over 45 years af age, should have a proctoscopic examination annually. Unlike cancer of the stomach, which more frequently affects males than females, cancer of the rectum and colon are equally frequent in both sexes.

Moreover, cancer of the colon and rectum, when diagnosed early and treated radically, have an excellent prognosis. As Dr. Boeck emphasized, a large number of cancers of the rectum are available to palpation with the digital finger. Annual sigmoidoscopic examinations for all patients over 45 years of age would succeed in uncovering many early lesions and would eliminate many unnecessary cancer deaths. Here, too, as in gastric cancer, I believe the cancer is there probably for approximately two years before it begins to cause symptoms —the usual length of the silent interval. Benign polyps which are frequent precursors of rectal as well as colic cancer may, however, bleed compelling examination before malignancy supervenes.

Now with reference to Dr. Boeck's specific question, for a cancer of the cecum or ascending colon, I advise and perform right hemicolectomy, together with enough ileum, usually about 15 to 20 cm.—to insure complete excision of the regional lymphatic drainage area. For cancers of the entire left colon as low as the juncture of the iliac colon and the rectum, and for cancers of the transverse colon beyond the hepatic flexure, I ordinarily do a total or subtotal colectomy, anastomosing the ileum or the ascending colon to the iliac colon or upper rectum. A fairly large number of such cases (approximately 70), have been done by me since the procedure was begun in 1946. Polyps in an area of the colon, removed from the primary lesion are uncovered in 38 per cent of the patients submitted to subtotal colectomy. Moreover, a silent cancer, removed from the primary lesion, also has been found in more than 5 per cent of the cases. Inasmuch as all the ileum remains, these patients do not have persistent diarrhea (Lilleher, R. and Wangensteen, O. H.: University Hospital Bulletin—Oct. 16, 1953). If, however, considerable ileum together with the right colon is removed, diarrhea usually follows. Incidentally, such a procedure is a wonderful operation for chronic constipation. I have done it a few times and have gained a few grateful patients in consequence.

William Lane of Guy's Hospital in London 40 years ago took out the left colon for exophthalmic goiter as well as for chronic intestinal stasis. Excision of the left colon, however, will not cure constipation. Lane, too, did occasional subtotal colectomies.

Dr. Halsted:—What do they do when they are cured of constipation?

Dr. Wangensteen:—Patients probably can find better uses for any time saved than spent trying to get their bowels to move.

Dr. Bailey:—You ought to hear about Dr. Brinkley's special colon washing.

Dr. Wangensteen:—I suppose every community has its Brinkley. I don't know your Brinkley. I, too, once did segmental resection of the left colon for

cancer. After having operated upon a patient for a cancer of the descending colon about 10 years ago, leaving a lesion in the iliac colon which the roentgenologist, proctologist and I all overlooked, making a secondary operation necessary a few months later—it was this experience which persuaded me to embark upon subtotal or total colectomy for left-sided colic cancer as a primary operation. There have been four deaths amongst those 70 patients—an operative mortality which compares quite favorably with that of segmental colic resection.

Dr. Boeck:—Do you ever make use of the proctoscope during surgery as a diagnostic procedure by opening the bowel and looking in both directions?

Dr. Wangensteen:—Yes, I have. The colon must be well prepared in order to do the procedure well at operation. Perhaps someone here has had greater experience than I with this technic.

Dr. Raymond Hedin of Red Wing, Minn., thought he could devise a proctoscope to inspect the colon from the anus to the splenic flexure. Maybe someday somebody will succeed in building a flexible sigmoidoscope which will permit doing this. I have interested an instrument maker in trying to build such an instrument.

Dr. Boeck:—When you have a cancer of the rectum, do you try in any of your cases, if you can, to preserve the sphincter?

Dr. Wangensteen:—Yes, I have overdone that, too. In the main, the adbominoperineal operation is better; the crux of the matter is that the lymphatic drainage area of every cancer *must* be removed. To remove the cancer widely without complete excision of the entire regional lymphatic drainage area is not enough. For cancers of the upper part of the rectum, near the junction of iliac, colon and rectum, I think the lymphatic drainage can be removed adequately so that it is safe to restore continuity. Below 10 cm. from the anus, one is rarely, if ever, warranted in attempting to save the sphincter. If he does, he may remove the lymphatic drainage area incompletely and fail to cure the cancer.

Dr. Boeck:—It is getting late. I don't know how long you men want to stay here. There is one thing I would like to ask Dr. Wangensteen with reference to cancer of the pancreas. Are we doing as many operations for cancer of the head of the pancreas as we started out to do, or are we folding up on that?

Dr. Wangensteen:—Radical pancreatoduodenectomy for cancer of the pancreas is one of the most difficult operations to do technically, because one has to restore the continuity of the bile duct as well as the pancreatic duct in order to have a functioning digestive system. My former associates, Dr. Clarence Dennis now in Brooklyn, and Dr. R. L. Varco of my clinic, are still enthusiastic over the radical operation for cancer of the pancreas. They have succeeded in doing this operation at a reasonable risk—something under 20 per cent mortality, which is not too bad for a fairly large series of cases. Moreover, they have a few relatively long survivors. Some surgeons I know, have capitulated to doing palliative

operations only, feeling that the operative mortality is too high. I do not know what the final answer is. Occasionally one sees a small cancer of the pancreas; a radical operation is done; the patient survives, and yet he dies before the expiration of five years of recurrent cancer. It would appear that the primary operation may not be radical enough.

Dr. Boeck:—Tell us about re-exploring these people.

Dr. Wangensteen:—In cancer of the colon there appears to be a good indication for taking a "second look" in patients found to have cancer in the regional lymph nodes at the first operation. In October, 1948, we embarked on this program and we have now submitted 28 patients with cancer of the colon, who were lymph node positive to "second look" operations.

On re-exploration, 14 of these 28 patients were found to be cancer negative. In other words, we had done a complete cancer operation and there were no residuals in 50 per cent of the patients who were lymph node positive at the time of the primary operation. Those 14 patients have all remained well. The "second look" procedure in cancer of the colon has prognostic value, too. The 14 remaining patients had residual evidence of cancer at the "second look" operation. Of these 14 patients, all of whom obviously would have succumbed eventually to residual cancer, four have become cancer negative through the principle of reoperation. It took six operations in one patient to effect the conversion. It took four operations in two patients and three in another patient. All have remained well.

I have also done the "second look" procedure for a few patients with "limited carcinosis". Confession is good for the soul. I think one mark of a strong man is the capacity to take a beating once in a while rather than to administer one. Anyone who is trying to cure cancer by surgery in the presence of carcinosis is obviously doomed to many defeats. Nevertheless, I have two patients, one with cancer of the ovary, the other with cancer of the colon. One of these patients had seven operations before she became cancer negative. In fact, I began to employ surgery as a suppressive agent for limited carcinosis in September, 1944, four years before I undertook the procedure for lymph node positive cancer cases. My first patient of this type was a nurse, a Miss E. J., Univ. Hosp. #747377, upon whom I first operated in September, 1944. We did not then reoperate as early as six months after the first operation as we presently do in the "second look" procedure. In fact, Miss E. J. would not let me do the reoperations until she thought symptoms had recurred. In seven years, I operated upon her seven times and succeeded in localizing the lesions finally to the right lower quadrant of the abdomen. Premature placement of a fascial graft in the abdominal wall to correct a large hernia seemed to give renewed vigor to the cancer, and it got out of hand.

The reoperation is done in the lymph node positive cases at intervals of six months, that is before the reassertion of symptoms. Our experience has been

that, the length of the silent interval in visceral cancer, before the recurrence of symptoms—when microscopic cancer has been left at an earlier operation, is in the area of 20 months. We have also converted a few lymph node positive gastric cancers through the agency of the "second look" procedure. But cancer of the colon constitutes the best indication for use of the "second-look" operation.

Some of you might ask: What is your control? Was the initial operation radical enough? I believe we do have satisfactory answers to these queries. We have done the "second look" operation on seven extensive Dukes' B cancers of the colon in which the lymph nodes were negative. One of these seven patients has died of pulmonary metastases without evidence of abdominal recurrence. The remaining six are well. No surgeons routinely excise the para-vena cava and the para-aortic lymph node chains at the primary operation. These lymph nodes are often found to be involved at the first "second look" procedure.

Dr. Boeck:—Well, I think we will call it a day. I have enjoyed participating in this and I want to thank you.

CLINICAL STUDIES OF BLOOD LIPID METABOLISM*

X. Serum Lipid Partitions in Metabolic Diseases

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Many publications recently in both the medical and lay journals speak of the significance of lipid changes upon the health in general. Our previous publications were concerned with the clinical significance of serum lipid changes in normals[1], peptic ulcer[2], recurrent myocardial infarction[3], atherosclerosis[4], chronic coronary artery disease[5], acute myocardial infarction[6], and liver diseases with and without jaundice[7]. The present studies concern themselves with "metabolic" diseases such as obesity, myxedema, hyperthyroidism, nephrotic syndrome, Kimmelstiel-Wilson syndrome, diabetes mellitus, cholelithiasis, castration, anemia, and xanthomatoses.

The purpose of this study was to determine the changes produced in the serum lipid partitions in patients with the above mentioned metabolic diseases and of what aid they may be for the clinician at the bedside in diagnosing and understanding the underlying pathologic physiology.

Method of Study and Material

The patients were all hospitalized except for a few with the diagnosis of simple obesity. They ranged in age from 30 to 89 years, of which 60 were male and 30 female. No food or liquids were permitted after the evening meal of the preceding day. Fasting, nonoxalated blood was obtained the following morning, being certain that the patient was at ease, not following any exercise or effort. Duplicate samples were determined. The lipid phosphorus (lipid esters of phosphoric acid) was determined by the Youngburg modified digestive method[8]. Phospholipid values were obtained by multiplying the lipid phosphorus determinations by the factor 25. Total lipids were determined by the gravimetric method (modified Bloor[9]). Total cholesterol and esters were determined by the Leiboff method[10]. In order to express the value of cholesterol esters in terms of actual weight, a factor of 1.67 was utilized. This figure was obtained by dividing the molecular weight of cholesterol oleate by the molecular weight of cholesterol. Neutral fats were obtained indirectly by subtracting from the total

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lipid values, the weights of the phospholipids, free cholesterol, and cholesterol oleate fractions. Lipid fraction percentages were calculated by dividing the weights of the various lipid fractions by the total lipids[1]. Liver function methods performed were the thymol turbidity test by Maclagan[11], cephalin-cholesterol flocculation test of Hanger[12], and total protein, albumin and globulin values by the tyrosine method of Greenberg[13]. Sedimentation values were performed by the Westergren method[14]. Height, weight and type of constitution were noted. Definitions, functions of lipid partitions, normal values, and detailed explanations of the methods were discussed in a previous publication[1].

The 90 patients studied included the following:

TABLE I

Clinical Condition	No. of Patients
Obesity	12
Myxedema	10
Hyperthyroidism	10
Nephrotic Syndrome	8
Kimmelstiel-Wilson Syndrome	6
Diabetes Mellitus (uncomplicated)	12
Cholelithiasis (uncomplicated)	10
Castration	5
Anemia	
Acute	6
Chronic	6
Xanthomatoses	5

Results

Obesity:—Twelve patients suffering from obesity, who were definitely determined to be on a nonendocrine basis, ranging in weight from 190 to 270 pounds, with an average weight of 218 pounds were studied. No other complicating medical diseases were noted. The results showed that the total lipids were less than normal (861 mg. per cent), averaging 839 mg. per cent. The phospholipids were slightly below normal (218 mg. per cent), averaging 210 mg. per cent. The total cholesterol is slightly above normal (197 mg. per cent), averaging 208 mg. per cent. The percentage of the cholesterol partitions is within normal range, as well as the neutral fats. The ratio of phospholipids to cholesterol is 1.15 and of cholesterol to phospholipids 0.86, both of which are normal (Table II and Fig. 1).

Myxedema:—Ten patients suffering from myxedema, ranging from moderate to severe, showed an increase of total lipids to 1,266 mg. per cent compared to normal of 861 mg. per cent. The phospholipids increased to 316 mg. per cent (normal 218 mg. per cent). Total cholesterol (324 mg. per cent) was markedly above normal. Although the total cholesterol is markedly increased, the cholesterol partitions revealed a normal percentage range. Fraction percentage evidently showed the increase of the lipid partitions to be due mostly

to ester and phospholipids rather than the neutral fats which showed a percentage value less than the normal range. It is interesting to note that the ratio of the phospholipids to cholesterol and the ratio of cholesterol to phospholipids were both normal (Table II and Fig. 1).

Hyperthyroidism:—Serum lipid partition studies in our series of cases were within normal limits (Table II and Fig. 1).

Nephrotic Syndrome:—Eight patients with nephrotic syndrome were studied in this series. There was an increase of all serum lipid partitions in this condition. Total lipid values were approxmiately three times normal. The total cholesterol is proportionately more increased than the increased phospholipids.

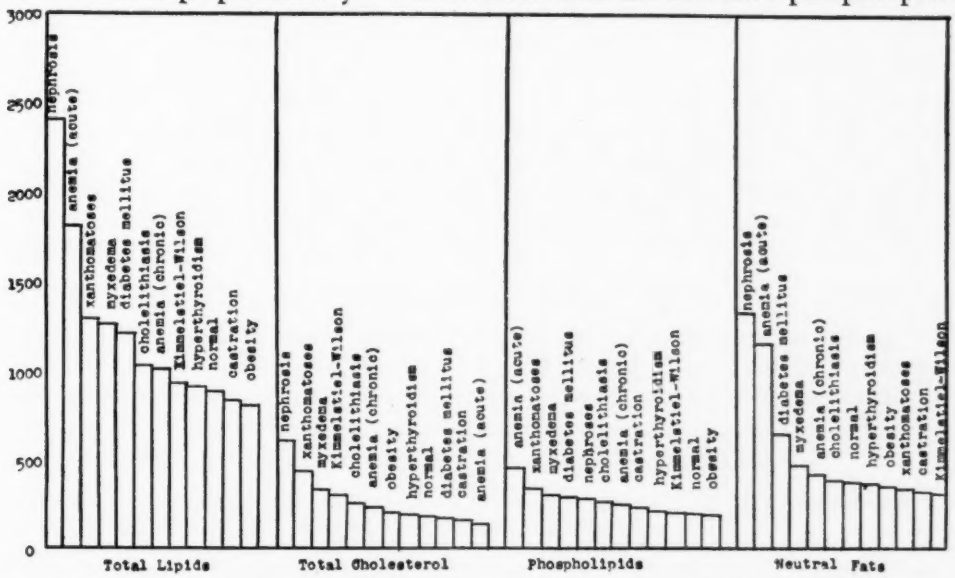

Fig. 1—Histogram showing the arithmetic mean values of serum lipid partitions in varied metabolic diseases compared to normal. Mg. per 100 c.c. as determined.

Evidently the increased total cholesterol is due to an increase of the free cholesterol rather than the esterified cholesterol. The lipid fraction percentage shows an increase of free cholesterol and neutral fats with a slight diminution of the esterified cholesterol and a markedly diminished phospholipids of approximately 60 per cent less than normal. This shows that there is no concomitant increase of the same degree of the phospholipids to the total cholesterol, and therefore explains why the blood serum in chronic nephrosis is usually cloudy or milky in appearance. It is agreed by all that one of the functions of phospholipids is to maintain a state of colloidal equilibrium for cholesterol[1]. This is further demonstrated by the fact that the ratio of phospholipids to cholesterol was the lowest obtained in the entire series of metabolic cases, namely 0.46. The ratio of cholesterol to phospholipids was the highest, namely 2.16 (Table II and Fig. 1).

Kimmelstiel-Wilson Syndrome:—Six patients with this syndrome were studied. The patients had no evidence of the nephrotic syndrome; the laboratory data pointed toward diabetes mellitus. The blood results showed an increase of all total lipids. The total cholesterol showed a greater increase than the phospholipids. The neutral fats were lower than normal. The lipid fraction percentage showed the free and esterified cholesterol to be above normal while the phospholipids and neutral fats were below normal. The latter was practically

TABLE II

ARITHMETIC MEAN VALUES OF SERUM LIPID PARTITIONS IN VARIED METABOLIC STATES COMPARED TO NORMALS

No. Cases	Diagnosis	Total Lipids	Lipid Phosphorus	Phospho-lipids	Cholesterol						Neutral Fats	Lipid Fraction %				Ratio	
					Total	Ester	% Total	Esterified as Oleate	Free	% Total		Free	Esterified as Oleate	Phospho-lipids	Neutral Fats	ph/ch	ch/ph
	Normals	861	8.6	218	197	121	61.2	202	76	38.8	365	9.1	23.5	25.3	42.1	1.10	0.90
12	Obesity	839	8.4	210	208	128	61.6	260	76	38.3	362	8.5	25.6	26.9	40.0	1.15	0.86
10	Myxedema	1266	12.6	316	324	197	63.0	323	127	37.0	463	10.4	30.8	26.6	35.7	1.00	0.97
10	Hyper-thyroid	893	9.5	238	199	137	68.0	229	62	32.0	364	7.1	25.6	26.6	40.7	1.19	0.83
8	Nephrosis	2412	11.0	275	595	324	54.0	541	271	46.0	1325	11.3	22.4	11.4	54.9	0.46	2.16
6	Kim-Wilson	910	8.9	222	320	210	65.0	351	110	35.0	227	12.0	38.5	24.4	25.1	0.69	1.44
12	Diab. Mellitus	1208	11.2	280	193	140	72.0	233	53	28.0	642	4.6	19.2	23.1	53.1	1.45	0.68
10	Cholelithi-asis	1010	10.9	274	258	166	65.2	277	91	36.2	368	9.3	27.1	27.3	36.2	1.07	0.93
6	Anemia (acute)	1800	19.8	450	140	90	64.0	150	50	36.0	1150	2.9	8.3	25.0	63.8	3.01	0.31
6	Anemia (chr.)	997	10.1	252	239	148	67.0	247	91	33.0	407	9.3	24.7	25.2	40.8	1.05	0.94
5	Castration	843	9.8	245	190	120	63.0	200	70	37.0	328	8.4	23.7	29.0	38.9	1.28	0.77
5	Xanthoma-toses	1274	13 0	326	408	264	67.0	440	144	33.0	360	10.7	33.5	25.9	29.8	0.99	1.16

60 per cent less than our normal values. There was a proportionately slower increase of phospholipids to total cholesterol. This was evident in the low ratio of phospholipids to cholesterol of 0.69, and of cholesterol to phospholipids of 1.44.

The plasma cholesterol concentration varies considerably in patients with chronic glomerulonephritis and other forms of renal disease[15]. The acute and

chronic active stages of glomerulonephritis are not infrequently accompanied by an increase in the plasma cholesterol concentration. The interesting findings in this Kimmelstel-Wilson syndrome undoubtedly are due to the diabetes mellitus with its tendency to glomerulosclerosis[16,17]. Although there was no edema present as in nephrosis, we note that the increase of the total lipids was caused by different factors, namely, that in nephrosis there was a marked increase of neutral fats and free cholesterol while in Kimmelstiel-Wilson syndrome there was a marked decrease of the neutral fats and a marked increase of the esterified cholesterol. This further corroborates the statements of the writers in their previous publications that determinations of the varied serum lipid partitions must be made to explain underlying disturbances[1].

Diabetes Mellitus (*uncomplicated*):—In twelve patients with diabetes mellitus studied, it was noted that there was an increase of total lipids to almost 1½ times normal. This is not due to an increase of total cholesterol, but to a very marked increase in the neutral fats (61 per cent above normal). There was a slight increase of the phospholipids. The ester partition was slightly above normal but the free esters were diminished. The lipid fraction percentage showed a marked increase of the neutral fats but practically a diminution of the other partitions (Table II and Fig. 1).

Cholelithiasis (*uncomplicated*):—The average results from our patients with cholelithiasis showed an increase of all the serum lipid partitions. The neutral fats were the least increased of all the lipids. The cholesterol partitions showed a normal ratio, particularly of the esters, thereby demonstrating no hepatic disturbance. Lipid fraction percentage revealed the maximum increase in the esters and phospholipids. It is of interest to note that the neutral fat percentage is less than normal. The ratio of phospholipids to cholesterol and vice versa were within normal range (Table II and Fig. 1).

Castration Syndrome:—Five patients with a castration syndrome were observed. There were no significant changes in the serum lipid partitions (Table II and Fig. 1).

Anemia (*acute and chronic states*):—In our series of 12 patients, six patients had severe blood loss of acute origin; while six patients suffered from chronic hypochromic anemia. In the former the total lipids were increased to approximately 2½ times normal, due mostly to the marked increase of neutral fats to 3.4 times the normal. The phospholipids increased at a faster rate (450 mg. per 100 c.c.) than the total cholesterol (140 mg. per 100 c.c.). This is evident by the high ratio of phospholipids to cholesterol (3.01) than normally (1.10). These lipid changes may be due to oxygen want and the marked liver dysfunction evident by the abnormal liver function tests.

The chronic anemic patients showed an increase of all serum lipid partitions, less marked than those encountered in the acute anemias. The neutral fat increased to only about 25 per cent of that of normals. The increased serum lipid

phosphorus and cholesterol is similar to a chronic anemia produced in animals by repeated bleedings.

Xanthomatoses:—Five patients with xanthomatoses were studied. They showed a marked increase of total lipids from 1½ to twice normal values. There was an increase of all the lipid partitions, except neutral fats which was only slightly decreased to 360 mg. per cent as compared to the normal value of 365 mg. per cent. The absence of increased neutral fat would exclude idiopathic (essential) hyperlipemia[18].

Liver Function Tests:—In general, all the liver function tests were within normal range as mentioned in our previous publications of lipid studies[2,3,6,7]. The liver played no significant role in the results obtained, except acute anemia which had a mean total protein of 4.76 gm. per 100 c.c.; xanthomatosis which had a mean value of 5.88 gm. per 100 c.c., and patients with hyperthyroidism with a mean value of 5.28 gm. per 100 c.c. Obesity showed no abnormal findings as obtained by some observers[19].

Discussion

Metabolism in General:—Metabolism is a sum total of tissue activity as considered in terms of physicochemical changes associated with and regulated by the availability, utilization, and disposal of protein, fat, carbohydrate, vitamins, minerals, water, and the influences which the endocrines exert on these processes[20]. Metabolic activities may be divided into two groups: one of anabolism or assimilation; the other of catabolism or disintegration. Alterations from these normal metabolic processes constitute diseases of metabolism. The details of metabolic processes differ among various cells, but in all it involves oxygen consumption, CO_2 and heat liberation, by enzymatic mechanism. The minimum heat production of the body, measured indirectly is the basal metabolism. Probably all cells utilize glucose in basal activity. Fats and proteins, however, also serve as a source of energy, especially when carbohydrates are not available[21]. That phase of biologic science which deals with the chemical transformation of foodstuffs in the body is referred to as intermediary metabolism[22].

Lipid Metabolism:—Our present discussion must concern itself only with a disturbance of lipid partitions in certain metabolic diseases. It is beyond the scope of this presentation and an impossible task to mention the disturbances produced by the other factors as carbohydrates, proteins, vitamins, endocrines, electrolytes, etc.

Dietary Fat:—The chief function of dietary fat is to promote a large available reserve of food and essential fatty acids to the organism. Cholesterol is an important means of transportation of fatty acids in the body especially through the formation of cholesterol esters[1]. The liver esterifies, synthesizes, stores, and destroys cholesterol. The liver acts as a starting point for fatty acids[23]. Phospho-

lipids, found in all living tissues, play a role in the permeability of cell membrane, muscular activity and in the function of the nervous system. Phospholipids determine the stabilization of serum lipid emulsions. They are synthesized in the liver which is concerned with their utilization.

Normal blood contains a cholesterol esterase which may be responsible for maintaining the normal ratio of free cholesterol to cholesterol ester. The body can synthesize cholesterol from any type of diet. The reticulo-endothelial system constitutes the type of cells lining the endothelium of the capillaries, the blood, the lymph sinuses of the hematopoietic organs, the stellate Kupffer cells of the liver, in the adrenals, and pituitary[24]. In general, the function is phagocytosis, storage (such as fat or lipids) hematological, blood cell formation (monocytes) and bilirubin formation from hemoglobin.

The liver may be considered as the organ for a common metabolic denominator in the stabilization of lipid metabolism[4]. All serum lipid abnormalities directly or indirectly associated with hypothyroidism, pituitary disorders, adrenal cortical or estrogen excess, and even metabolic disturbances as diabetes mellitus are mediated through the liver. Excess fat intake, inadequate protein and inadequate Vitamin B-complex, including lipoproteins may be manifested clinically through liver dysfunction[4]. Some investigators[25] maintain that metabolic changes during shock and stress may even be due to liver dysfunction. Hormones affect the rate of intermediate metabolism within certain cells, thereby controlling their function. Hormones may act by changing cellular permeability and intracellular organization or by affecting specific steps in intermediary metabolism. Endocrinopathies are considered by some as disorders of metabolism[26].

Metabolic Diseases Studied

Obesity:—Obesity is a very important clinical condition for the clinician. The fear instilled into patients reading current medical and lay literature on this subject has become a topic for daily discussion. The patient, however, needs to be informed of the increasingly detrimental influence of obesity as age advances, of the statistical evidence that obesity adversely affects longevity, of the mechanism involved in its causation (frequently psychogenic excessive food consumption), and of the ill effects upon the cardiovascular apparatus[27]. There is no good experimental data to indicate that simple obesity is due to any abnormal metabolic process, to account for the accumulation of fat. In fact, the energy exchange in the basal state, as well as the expenditure of energy during work is greater in the obese than in normal people of similar age, height, and sex, under the same conditions[28].

Obesity may be due to nervous system abnormalities due to endocrine disturbances. In the latter the pituitary is at fault. Generally, obesity due to errors of diet may be classified into the plethoric and the anemic types. The basal

metabolism in obesity is, as a rule, unchanged. The liver becomes not only a manufacturing area of fat, but also a storehouse. The chemical properties of fats are very much changed in digestion. The intestine possesses the power to modify the composition of fat during this absorption. The blood fat is transported to three places: first, the tissues; second, the liver; and third, the depots for fat. The fat in the liver is available for energy[29]. Obesity is moderately associated with Sf 35-100 lipoproteins[30] and less so with an increased total cholesterol. Obesity, therefore should be energetically treated[31].

Myxedema:—Myxedema is a state of hypothyroidism, a condition consequent upon the failure of the thyroid gland to elaborate its specific hormone. Myxedema is part of such a condition. The clinical features are usually characteristic and not difficult to diagnose. Usually the basal metabolism rate is diminished; the blood cholesterol is elevated, and the total value for the proteins is increased. The differential diagnosis should include pernicious anemia, chronic nephritis and the myxedema heart. The underlying pathology is due to a primary atrophy of the thyroid gland, increased storage of proteins, and water in the intercellular spaces, on the one hand, and a decrease in a normal range of tissue metabolism, on the other hand[32].

Usually patients with myxedema may show an increase of lipids, dependent upon hyperactivity of the anterior hypophysis secondary to the diminished thyroid function, since it does not develop in hypophysectomized-thyroidectomized animals. A return to normal usually follows the administration of thyroid extract. There is evidence that the thyroid hormone influences the distribution of cholesterol between the plasma and tissues, rather than the synthesis and destruction of cholesterol[33].

Hyperthyroidism:—Ten patients with a diagnosis of hyperthyroidism were studied. In thyroid diseases there appears to be a rough reciprocal relationship between the basal metabolic rate and plasma cholesterol concentration[34]. Low values may be obtained in patients in or near thyroid crisis. With the present day advancement of diagnostic acumen, the cholesterol value, and even to a certain extent, the basal metabolic rate are not considered wholly diagnostic of such a state. Radioactive iodine uptake and urinary excretion studies are more accurate of a pathological state. The severity of the hyperthyroidism will determine the clinical, chemical and laboratory findings.

Nephrotic Syndrome:—The term usually applied to degenerative diseases of the kidney, as opposed to inflammatory is designated as nephrosis. This term refers to lipoid or genuine nephrosis, which shows a fatty degeneration of the tubules of the kidney and degenerative changes in the glomeruli. The laboratory findings usually show marked albuminuria, edema, hypercholesterolemia, reduction of the total plasma protein with inversion of the albumin-globulin ratio, and the presence of doubly refracting lipoids in the urinary sediment. The significance of this phenomenon and the factors responsible for its development

are not clearly understood. Its association with the diminished concentration of serum protein, and particularly serum albumin, suggests the possibility that both phenomena may be concomitant if not related features of some underlying metabolic disorder. It has been suggested that the lipemia of the nephrotic syndrome may represent an attempt to maintain the osmotic pressure of the blood plasma which is lowered as a result of diminution in serum protein. Some attribute the hypercholesterolemia of the nephrotic syndrome to some defect in the mechanism which ordinarily removes cholesterol from the blood or to some disturbance which causes excessive mobilization of lipids from the fat depots[35]. It may depend upon diminution in the activity of the reticulo-endothelial system in removing cholesterol from the blood, resulting from alteration in the colloidal state of the plasma due to diminution in its protein content[36].

Kimmelstiel-Wilson Syndrome:–This syndrome also called intercapillary glomerulosclerosis, usually occurs in individuals with long standing diabetes and may occur even though the diabetic state is mild. It may also occur in the absence of diabetes. The pathology shows noninflammatory focal fibrosis of the glomerular tufts. Clinically, one may encounter massive proteinuria, hypoproteinemia, edema, and hypertension without such a syndrome. The condition therefore bears a close resemblance to the subacute or nephrotic state of chronic glomerulonephritis. History in a middle-aged hypertensive diabetic patient with definite urinary findings will be of help in the differential diagnosis.

In the Kimmelstiel-Wilson syndrome, the increased lipids were due especially to the ester fraction of total cholesterol, while the phospholipids were just above normal. The neutral fats were below normal in contrast to the nephrotic syndrome wherein the increased neutral fats were responsible for the lipid changes. This condition must be differentiated from intracapillary glomerulonephritis, a rare form of glomerulonephritis and is usually associated with a nephrotic syndrome[37]. It is sometimes spoken of as lobular glomerulonephritis[38].

Diabetes Mellitus (uncomplicated):–It is generally recognized that lipemia may occur in diabetes mellitus[39,40]. In the great majority of cases the hypercholesterolemia of diabetes mellitus is due to an approximate proportinate increase in both the free and esterified fractions[41]. The factors underlying the development of hypercholesterolemia in diabetes mellitus are not very well understood. In view of the fact that although absorption and oxidation of lipids are unimpaired in diabetes, lipemia is rather consistently associated with that condition. It probably represents an abnormal localization of lipids in the blood rather than any impairment of lipid metabolic processes. It may be that diabetic lipemia is a reflection of the increased metabolism of fat because of the unavailability of carbohydrates, being similar therefore to the lipemia of starvation[42]. Hemoconcentration may be a factor in producing an increase of lipid partitions[43]. It may also be due to an increased production of the acetate compounds incident to the increased metabolism of fats[44].

Our cases show an increased total cholesterol need not always be present in patients with diabetes mellitus (not complicated by the presence of diabetic coma and severe acidosis). Hypercholesterolemia may be produced in diabetic patients by a high fat intake, undernutrition, severe acidosis and coma[42]. None of our cases were accompanied by the aforementioned complications. It is worthy to reemphasize that our cases of diabetes mellitus showed a slightly increased range of the esters and a diminution of the free partitions of cholesterol. This is mentioned because of the recent work claiming that most diabetics have hepatic disturbances such as fatty liver and cirrhosis[45,46]. Since esterification is a function of the liver, the normal or slightly increased cholesterol ester shown by us would not be evident of any underlying severe damage and disturbances to liver function. Attention may be called, since diabetes is prone to accompanying vascular changes, such as coronary artery disease and atherosclerosis, to the expectation of a lower ratio of phospholipids to cholesterol and conversely so. Indeed our ratio of phospholipids to cholesterol was much above normal, 1.45, while that of cholesterol to phospholipids was 0.68 (Table II and Fig. 1).

Cholelithiasis (uncomplicated):—Ten patients with cholelithiasis, without any complications such as hepatitis and jaundice were studied. It is the opinion of the authors that gallstones may be formed simply from excessive concentration of bile due to a prolonged stay in a noninflamed gallbladder. Consequently, there is a precipitation or a caking-out of the bile constituents[47]. The concentration of cholesterol in the human gallbladder is so much greater than that ever attained in the blood that it seems impossible that hypercholesterolemia may be the only factor in the formation of gallstones. An inflamed gallbladder mucosa produces relatively large quantities of cholesterol in the contained bile with a secondary effect upon the liver, which may produce a hypercholesterolemia[48]. The hypothesis of the relationship of cause and effect between hypercholesterolemia and cholelithiasis has not been substantiated by recent investigations. Occasionally hypercholesterolemia may be encountered in patients with cholelithiasis without obstruction of the common bile duct. This hypercholesterolemia is thought to be due to the absence of bile or some of its constituents from the intestines, which is the determining factor and the causation of this phenomenon. Others believe the hypercholesterolemia is due to increased rate of cholesterol synthesis in the liver[49]. We wish to repeat that an underlying hepatitis with or without jaundice may produce increased serum lipid partitions as previously published by us[7]. This condition is precluded as an underlying factor in producing the increased serum lipid partitions found in our patients with uncomplicated cholelithiasis. The possibility of a concurrent inflammatory process of the gallbladder may be an important factor in producing findings similar to ours, in addition to the increased cholesterol synthesis in the liver as mentioned above.

Castration:—There is a distinct tendency for the patient suffering from this syndrome to gain weight. Fat usually accumulates in the mammary region, over

the abdomen, about the mons pubis and around the hips. The thyroid gland, usually is not enlarged and the basal metabolic rate tends to be depressed. Blood cholesterol is generally high in hypogonadism associated with hypometabolism. Whether castration is evidence of hypothyroidism has not been determined. The clinical signs of hypothyroidism are ordinarily not seen in castrated patients. Experimentally, profound changes occur in the pituitary gland after castration. It becomes larger, hyperemic and markedly increased in physiologic activity. The thyroid gland acts as an antagonist to testicular hormones. There is a distinct change in the size of the adrenals in castrated rats[50]. Experiments have demonstrated that the fat content of the castrated animals is increased and that the extra fat is deposited interstitially as neutral fat. The increased fat is considered to be due to a secondary process of muscle protein changes[51].

Anemia (acute and chronic states):—The values of the serum lipid partitions will vary proportionally to the intensity and the acuteness of blood loss. Acute anemia may show high total lipids by the increased neutral fats and phospholipids. While chronic states of anemia may have lipid values slightly above the average normals, they are less than the acute anemic state by lower phospholipids and neutral fats. The cause of the increase in plasma cholesterol is not known. The suggestion has been advanced that it may be due to a loss of plasma proteins, representing an attempt to maintain the colloid osmotic pressure of the plasma at a normal value. There is little evidence to substantiate this hypothesis. It may be due to either decreased oxidation resulting from the diminution in erythrocytes or to excessive mobilization of lipids from fat reserves in the tissues[52]. The variations of serum lipid partitions observed may be due to associated or coincident metabolic disorders rather than to any specific relationship to the diseases in question. The oxygen want, anoxemia, the acuteness and chronicity may be important factors to be considered for the marked variations obtained and observed.

Xanthomatoses:—(Lipoidosis or abnormal deposits of lipids). A group of diseases wherein the reticulo-endothelial system in various tissues or organs take up lipids to produce diffuse infiltrations or even large tumor masses. These conditions are usually spoken of as lipomatoses, because of a yellow color which characterizes many of them. Lipoidoses by Thannhauser[53] is a more appropriate term. Xanthomatoses is reserved for those conditions in which cholesterol is the predominant lipid in the tumors or infiltrations. The cholesterol appears chiefly in the form of esters. Thannhauser divides them into primary and secondary xanthomatoses.

Primary Xanthomatoses:—These usually are accompanied by hypercholesterolemia, characterized by accumulation of foam cells of a tumorous nature in certain kinds of tissues, especially in tendons and skin or subcutaneous tissues (xanthoma tuberosa or plana). The neutral fat remains normal. Usually there is no response to diet.

Secondary Xanthomatoses:—This occurs as a secondary phenomenon of some other disease which is accompanied by hyperlipemia, e.g., diabetes mellitus, which has lipid deposits scattered in the skin and essential hyperlipemia. The latter is also known as idiopathic familial lipemia and hepatosplenomegalic lipoidosis. This is a disorder of fat metabolism of undetermined origin characterized by hyperlipemia of the retention type, frequently accompanied by hepatosplenomegaly, eruptive xanthomatoses and abdominal pains. The increase in blood lipids is due mostly to a rise of the concentration of neutral fats[54]. Xanthomatous biliary cirrhosis (pericholangiolitic biliary cirrhosis) is an infiltration of the parenchyma of the liver and the bile duct with increased cholesterol and lecithin. It is considered a liver disorder. Possible hepatic lesions, like the skin lesions, are associated with the lipemia[55]. The tertiary group includes xanthomatoses usually not accompanied by hypercholesterolemia, for example: Hand-Schüller-Christian, Niemann-Pick's, Gaucher's, and Tay-Sachs Diseases.

The disorder may be relegated to the tissues where the lipids are deposited, but the reasons for its accumulation in these sites are quite as obscure. The peculiar localization in specific types of tissues in the absence of any demonstrable abnormality of serum lipid patterns and the response to local x-ray treatment argue against a disturbance of the general lipid metabolism.

Summary and Conclusions

1. Metabolism with its activities of anabolism and catabolism; intermediary metabolism have been discussed and defined.

2. The role of endocrine, liver, and reticulo-endothelial system to disturbances in lipid metabolism has been mentioned.

3. Serum lipid partitions have been studied in 90 male and female patients with metabolic disorders such as obesity, myxedema, hyperthyroidism, nephrotic syndrome, Kimmelstiel-Wilson syndrome, diabetes mellitus (uncomplicated), cholelithiasis (uncomplicated), castration, anemia (acute and chronic states) and xanthomatoses.

4. Increased total serum lipids were obtained in all the conditions except simple obesity, hyperthyroidism, and castration.

5. Endocrine glands will influence lipid changes in conditions such as myxedema, nephrotic syndrome, hyperthyroidism and castration.

6. Reticulo-endothelial system dysfuction produces lipid changes in the xanthomatoses and nephrotic syndrome.

7. Anoxemia and liver dysfunction will vary lipid values in acute anemic states.

8. Normocholesteremia may occur in castration, simple obesity and uncomplicated diabetes mellitus.

9. Increased total lipids may be caused by varied factors. The greatest increases were observed in nephrotic syndrome, acute anemia and xanthomatoses.

10. Malnutrition (in nephrosis), starvation, hemoconcentration (in diabetes mellitus), disturbed oxygen utlization by the tissues (thyroid) and stress (acute anemia) may be important factors in the production of the obtained results.

11. Liver function determinations were normal in metabolic diseases except in the acute stage of anemia and severe xanthomatoses.

12. The liver may be the organ for a common metabolic denominator in the stabilization of lipid metabolism.

13. The ratio of phospholipids to cholesterol and vice versa were found to be normal in metabolic diseases considered prone to atherosclerosis and chronic coronary artery disease.

14. The different serum lipid partitions must be determined to ascertain which may be the one affecting the underlying disturbance.

15. Varying results of serum lipid partitions obtained in this study preclude dogmatic denunciations by some observers.

Appreciation is expressed to our secretary Miss Dorothy Schork.

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NONPARASITIC CYST OF THE SPLEEN

A Case Report

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Cyst of the spleen is a rare condition, the literature was reviewed by Harmon and Chalmers in 1946 in which only 163 cases were recorded on that date. In Thailand this is the first case encountered. Different classification of various types histologically were made by many authors. For practical and clinical purposes it would seem sufficient to classify them as parasitic, true and false (Donovan, 1948).

Symptoms:—Cysts of the spleen usually are symptomless unless they become large enough to give pressure symptoms or are palpable. When symptoms occur they are usually nausea, vomiting, diarrhea, pain in the upper part of abdomen and rarely slight jaundice (Snoke, 1929).

Signs:—The following signs may be found:—Abdominal mass of varying sizes located in the upper left quadrant of abdomen, being cystic or firm depending on the nature of the cyst. Displacement of the abdominal viscera detected by physical examination or x-rays especially the stomach which may account for abdominal symptoms. The visualization of calcification of the cyst wall by x-rays in some instances (Scotson 1933, Shawan 1937).

Differential Diagnosis:—In every instance the tumor mass of the stomach, left kidney, left adrenal, left colic flexure and possibly ovarian cyst have to be ruled out. The splenic cyst, on palpation, moves with the spleen during respiration. In cases with calcification the aneurysm of the splenic artery with calcification may closely resemble the picture. Auscultation over the tumor may reveal the presence of a bruit and angiography may also be an aid to clarifying the diagnosis. The calcification of the spleen seen in other conditions such as gout, tuberculosis, trauma or arteriosclerosis may be easily ruled out (Shawan 1937).

Treatment:—The treatment of a splenic cyst is surgical removal of the spleen after thorough study of blood and marrow to determine the resectibility.

Case Report:—A. N. 9989-95 H. N. 36966-95. A multiparous Thai female aged 38 was admitted to the Gynecological Department, Siriraj Hospital, Bangkok,

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Thailand, on September 5, 1952 with the chief complaint of having a mass in the left hypochondrium for eight years. The present history dates back to the time when she developed a small, painless, flat mass projecting under the lower margin of the last rib. The mass gradually increased in size day by day without producing any discomfort until the lower margin of the mass reached the umbilical region two years ago with subsequent development of pressure in the abdomen. The mass was firm and very slow growing. Two months prior to admission she noticed another mass lying anteriorly to the former. This mass increased in size rapidly, reaching the size of a fetal head on admission. The history of pain, trauma, manipulation of the original mass were negative at the onset of the development of the second mass. Finally, the mass bulged out and became protuberant. The patient took various herbal medicines without beneficial effect then she was brought in for hospitalization. The past history revealed malaria five years ago.

Fig. 1—Photograph of the gross specimen of the spleen showing the cyst intact, the 3 indentations are caused by artifact.

Physical examination on admission revealed an undernourished female with enlarged protuberant abdomen. Temperature 37° C. Pulse 80 per min., Respiration 20 per min., B.P. 110/70. The abdomen showed a bulging cystic mass about the size of a fetal head in the left hypochondriac and lumbar regions. Palpation revealed two masses adhered to each other. The deeper one occupied the left flank, being firm and moved with respiration. The upper one was cystic, globular and bulging. Pain and tenderness were absent on deep pressure. The liver was not palpable. Pelvic examination by Prof. Term Bunnag revealed *multiparous introitus* with transverse laceration of the cervix. The uterus was retroflexed, the size of which could not be determined. The left side of abdomen was occupied by a large irregular mass with protrusion of the lower pole into the cul-de-sac. Impression from the examination was that of a multilocular ovarian cyst with splenomegaly. The case was referred to the

Medical Department for corroborative diagnosis. Complete hematologic study was done and showed 6.1 gm. hemoglobin, R.B.C. 2,080,000, W.B.C. 4,100, platelets 209,600, reticulocyte 1 per cent, fragility test was normal. Sternal puncture was performed in September 1952. Bone marrow:—Numerous clumps obtained, hypercellular with well-matured myeloid series, normal erythroid elements, and numerous megakarocytes. Marrow was not diagnostic. Owing to the character, position and consistency of the mass, the diagnosis of splenic cyst, associated with Banti's disease, was made by the authors. Exploratory laparotomy with the possibility of splenic resection was advised. The patient was operated on Sept. 30, 1952 with the following findings:

The abdomen was opened by a median incision, extending from about 3 cm. below the xiphoid process to just above the symphysis pubis. The length of the incision was about 24 cm. long.

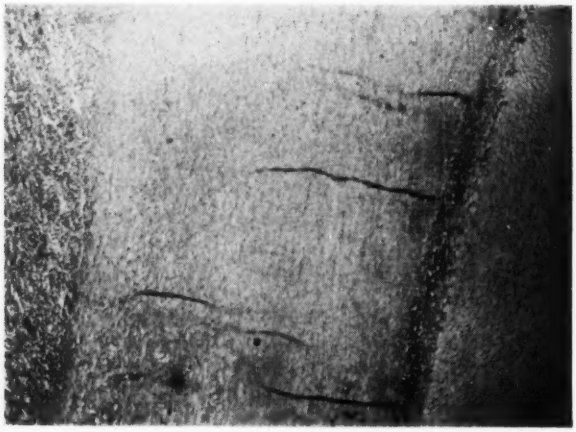

Fig. 2—Photomicrograph (x40 magnification) showing the cyst wall and part of splenic tissue.

On opening into the peritoneal cavity, the spleen was found to be about 10 times larger than its normal size, although it still retained its usual shape. The lower pole extended down to about 3 cm. below the iliac crest, and its right margin 5 cm. beyond the mid-sagittal line. On the anterior surface, there was a thin-walled cyst, measuring 18 cm. in diameter. There was slight omental adhesions to its right lower part, otherwise freely mobile.

The uterus was slightly enlarged, due to recent pregnancy, curetted 4 days prior to the operation. Other internal genital and abdominal organs appeared normal. There was no ascites.

Omental adhesions were separated and tied, and the spleen with its cyst was lifted out of the abdominal cavity with ease. The pedicle was clamped, tied and cut. The gastrosplenic and splenorenal ligaments were separated and the tumor was removed en masse.

The spleen together with the cyst measured 25 cm. in length 19 cm. in width and 12 cm. thickness, weighing 3,800 gm.

Macroscopic Examination:—The specimen consists of a spleen with unilocular thin-walled cyst. The cyst measures 10 x 16 x 20 cm. It is greatly enlarged, showing a thin smooth capsule. Cut sections show smooth dark brown splenic tissue. There is no evidence of infarction. The cyst is attached to the anterior surface and lower half of the spleen, and rests on the capsule of the spleen. It has a hemispherical shape and a thin fibrous wall. The content is of brownish gelatinous material (result of fixative).

Microscopic Examination:—Sections show hyperplasia of reticulum cells and lymphoid tissue. There is also an increase of fibrous tissue. Phagocytic cells are seen ingesting brown pigment. The spleen is separated from the cyst by a thin fibrous wall which is in direct continuation with the capsule of the spleen. The cyst is lined by flat endothelial cells. The content of the cyst shows homogenous acidophilic material with some cellular elements composed chiefly of lymphocytes.

Diagnosis:—Splenomegaly. Solitary serous cyst, extracapsular.

The postoperative course was uneventful and the patient was afebrile. She was discharged on October 16, 1952.

Comment:—Banti's disease is not a rare condition in Thailand, however, the development of an acquired serosanguinous cyst is a very unusual coexistence. The spleen in Banti's disease is friable and liable to trauma which may take place in certain instances unnoticed by the patient. The patient also exhibited unusual physical findings of two adherent masses of different character and consistency, one being flat, deeper and firm, the other globular, cystic and protuberant. The possibility of an ovarian cyst with a long pedicle adhered to the anterior surface of the spleen is more common. The ovarian cyst, however, should be adherent to the lower pole of the spleen or the posterior surface. By sound clinical judgment the case was diagnosed as a splenic cyst prior to operation. The possibility of an echinococcal cyst of the spleen also has to be considered although one case report of echinococcal cyst of the lung was reported in this country in an Indian immigrant. This disease, however, has never been present among the Thai population here, and the microscopical examination and character of the fluid from the cyst definitely ruled out this possibility.

Conclusion:—A case of acquired cyst of the spleen in co-existence with Banti's disease in a 38-year old Thai woman with interesting physical findings is presented.

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THE SURGICAL MANAGEMENT OF CONGENITAL MEGACOLON (HIRSCHSPRUNG'S DISEASE)*

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Within recent years, a better understanding of the basic pathologic physiology of the colon in Hirschsprung's Disease has resulted in a more rational surgical approach to effective treatment. The segmental character of the abnormal function of the large bowel, as determined by roentgenograms in this disease, has been quite consistent and has resulted in the development by the author of a corrective procedure which has been uniformly successful in the 18 cases treated to date.

Etiology

Since Hirschsprung's original paper[1] a great number of ingenious theories as to the cause of congenital megacolon have been presented. Their multiplicity indicated the failure of anyone to explain adequately the true nature of the disease.

In 1920 dalla Valle[2] called attention, for the first time, to the alteration of ganglion cells of the mysenteric plexus and the reports of a number of other authors since then substantiate the fact, that, in the narrowed rectosigmoid area and in a variable portion of the proximal dilated sigmoid colon there is an absence of ganglion cells[3-7]. As a result of these observations, the commonly accepted theory of the cause of congenital megacolon is that there is a functional obstruction at the level of the narrowed rectosigmoid area with secondary dilatation and hypertrophy of the proximal colon. Swenson[8,9] has also suggested that, in addition to the rectosigmoid area, the rectum, too, is abnormal in its behavior, and has devised a surgical procedure which entails removal of the narrowed rectosigmoid area, a variable portion of the dilated sigmoid colon, and the major part of the rectum, re-establishing bowel continuity by anastomosing the sigmoid colon to the small residual portion, using a "pull through" technic. As of December 31, 1951[10], at the Children's Hospital in Boston 70 patients were treated by the described operation with but 2 deaths. Of the surviving 68 patients, followed for periods varying from 8 months to 5 years, one patient has required a secondary removal of more bowel, three patients have required rather frequent enemas and in 6 others, occasional enemas have been needed to relieve temporary retention of feces.

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Functional Activity of the Bowels Determined by Roentgenograms

Neuhauser[11] first pointed out the important and key finding of the narrowed rectosigmoid area in all patients with true congenital megacolon. In all of our patients, this narrowed area of variable length has been present. Its absence virtually rules out the diagnosis. In addition we have noted the following roentgenographic findings (Fig. 1):

1. The rectum appears to have normal caliber and function.

Fig. 1—Roentgenographic findings in a nine year old patient with congenital megacolon. This x-ray shows particularly well: 1. the normal caliber of the rectum; 2. the "narrowed" rectosigmoid area; 3. marked dilatation and absence of haustral markings on the left side of the colon and 4. normal diameter and haustral pattern on the right side of the colon.
The transition area is somewhere in the mid-transverse colon. (*Reproduced by permission of Surgery, Gynecology and Obstetrics*)

2. The right side of the colon, i.e. the cecum, ascending, and variable extents of the transverse colon, present good haustral markings and evidence of good contractility.

3. The left side of the colon, i.e. portions of transverse, descending, and sigmoid colon, are markedly dilated, and show little if any evidence of haustral markings or peristaltic activity.

These three findings are extremely important. They have governed the extent of colonic resection in our cases. The narrowed rectosigmoid and portions of the colon, which show impaired peristaltic activity roentgenographically, are removed. The rectum is left and an anastomosis between it and the right side of the transverse or ascending colon, which shows good peristaltic activity, is carried out.

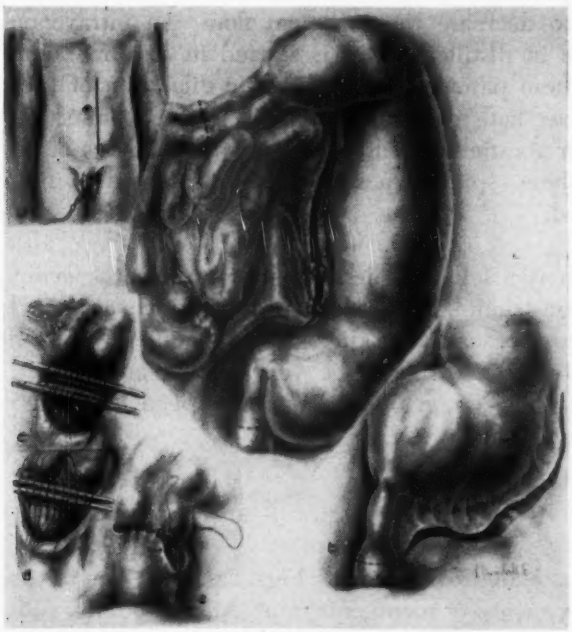

Fig. 2–Steps in the operative procedure. The central diagram shows the changes in the bowel seen at laparotomy, the extent of resection is indicated by dotted lines. The proximal line of resection is through a portion of the transverse colon which has normal bowel thickness and good haustrations. The distal line of resection is through the upper portion of the rectal ampulla, just distal to the "narrowed" rectosigmoid area. This is depicted more clearly in b. a. The type of incision used. Note also the inlying catheter. c, d, and e, details of the closed anastomosis used. In c, the posterior row of sutures has been placed. These are tied and cut. The clamps are rotated and the anterior row of sutures is inserted. The clamps are loosened and removed as the anterior row of sutures is tightened up to prevent spillage. They are then tied and cut. Reinforcing sutures are used as needed. e. Considerable care is taken to extraperitonealize the line of anastomosis. (*Reproduced by permission of Surgery, Gynecology and Obstetrics*)

Operative Procedure

Since these patients have suffered many years of chronic ill-health, their nutritional status is impaired and special attention has been directed towards getting them into the best possible condition for operation. They have received a high caloric diet with vitamin supplements and, where indicated, repeated whole blood and plasma transfusions have been given to elevate the plasma proteins and correct anemia. Attempts have been made to clean out the colon pre-

operatively, but vigorous administration of enemas is not necessary. In fact, it is undesirable for the child may become markedly weakened because of them. Since at the time of operation much of the content of the colon can be milked into the dilated sigmoid, which is to be removed, the presence of a moderate amount of feces in the colon does not interfere with the operative procedure. For three days prior to operation the patient is given aureomycin (neomycin more recently) orally, to decrease the intestinal flora. An intravenous injection of 5 per cent glucose in distilled water is started in an arm before operation and, since many of these patients have idiopathic dilatation of the urinary bladder, all patients have had urethral catheters inserted immediately after being anesthetized. For anesthesia, pentothal-curare solution has been used in all cases except one, where spinal anesthesia supplemented with pentothal-curare solution was used.

The incision is a left paramedian incision from the symphysis pubis well up into the epigastrium (Fig. 2a). In our first two cases a left hockey stick incision was used, because some difficulty in mobilizing the splenic flexure was anticipated, but it was found to be very mobile and offered no problem in dissection. Where the paramedian incision has been used, care has been taken to keep the rectus muscle intact.

Extent of Resection

The proximal extent of resection (Figs. 2a and b) in all cases is determined preoperatively by means of roentgenograms. At laparotomy, with the entire colon exposed, the findings corroborate those obtained by roentgenograms. The rectal ampulla has a normal thickness and diameter. The "narrowed" area between the rectum and dilated sigmoid is of variable length but has been present in all cases of true congenital megacolon. The definition between the dilated left side of the colon (sigmoid, descending, and variable portions of the left side of the transverse colon) and the right portion of the colon is often very clearly seen, particularly, if care is taken not to push gas and stool back from the dilated sigmoid on mobilization of the latter. The level of transection of the bowel on the right side can be readily identified, for at this level, the bowel has normal thickness and the longitudinal muscular bands are normally placed so as to produce haustrations. In fifteen cases this level of proximal transection has been in the right half of the transverse colon. In two, it has been in the ascending colon just proximal to the hepatic flexure and in the remaining one in the left side of the transverse colon. In all instances the colon is removed proximal to the most distal area of active peristalsis as determined fluoroscopically. This is done purposely so as to avoid any error in utilizing bowel of questionable peristaltic activity. Distally, the definition of the normal rectal ampulla has been made in all instances without difficulty and with as little dissection of the rectum as possible for two reasons:

1. The prevention of injury to the *nervi erigentes* and

2. avoidance of producing a large space between the rectum and hollow of the sacrum which predisposes to perirectal infection and leakage at the line of anastomosis.

A closed one layer type of anastomosis[12] is made, using Wangensteen's intestinal anastomosis clamps (Figs. 2c and d). Interrupted 40 silk sutures inserted in the Lembert fashion are used. Because of the good length of the rectal stump, there have been no particular technical difficulties with the

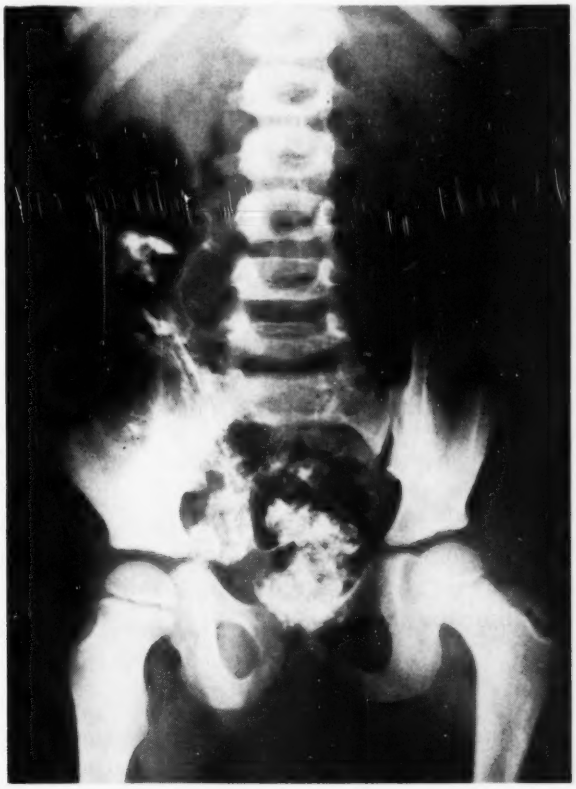

Fig. 3–Postoperative roentgenogram showing the degree of evacuation of the barium enema. The contractility of the remaining colon has resulted in almost complete evacuation of the barium. (Reproduced by permission of *Surgery, Gynecology and Obstetrics*).

anastomoses. The level of the anastomoses has been between 6 and 10 centimeters from the anal skin. Great care is taken to extraperitonealize the anastomosis (Fig. 2e).

In two patients difficulty was encountered in bringing down the transverse colon to the rectum because of unusual distance between the upper abdomen and pelvis. In these patients the middle colic artery was clamped at its origin and after the collateral circulation was found to be good the vessel was transected

and tied. This resulted in the needed additional lengtht to do the anastomosis without tension.

No attempt is made to close off the bare areas made by removing the descending and sigmoid colons and their respective mesenteries. One gram of streptomycin and 500,000 units of penicillin are deposited routinely within the peritoneal cavity at the level of anastomosis before closure. A tube is left in the stomach for decompression purposes for approximately 48 hours after operation. Closure of the abdominal wound is carried out using interrupted 30 silk (deknatal). Postoperatively these patients receive parenteral fluids, streptomycin and penicillin for the first four days. Early ambulation is practiced. The urethral catheter is removed on the third day and re-inserted if the residual urine is greater than 75 c.c.

Results

Eighteen patients, ranging from 2 to 21 years, have been operated, using the above described technic, with no operative mortality. The results in 17, followed for a period of six months to four years, have been excellent, in that they have daily bowel movements, without the use of enemas or cathartics. One patient, whose result can only be classified as good, developed several bouts of abdominal distention and constipation following surgery. He responded to enemas and again started having spontaneous bowel movements.

Postoperative roentgenograms of the residual colon in all cases except one (Fig. 3) have shown good peristaltic activity and emptying. There has been a marked improvement in the general health and physical endurance in all patients. In those who were still in the growing period there has been a gratifying increase in height and weight. The personalities of these patients have also improved in a dramatic fashion.

Comment

The theory that the basic defect of congenital megacolon rests entirely at the rectum and the narrowed rectosigmoid area, and that as a result of functional obstruction secondary dilatation of the proximal colon occurs, cannot be accepted without some question for the following reasons:

1. The absence of ganglion cells is encountered in variable portions of the dilated colon as well as in the narrowed rectosigmoid area.

2. The rectum, as visualized by roentgenograms, appears to be normal in size, shape, distensibility and contractibility.

3. If the changes in the bowel proximal to the "narrowed" area were secondary to obstruction above, one would expect the cecum, because it has the largest diameter of any portion of the colon, to have the maximum dilatation.

Certainly this is the picture in other instances of colonic obstruction of an incomplete and chronic character (e.g. carcinoma, diverticulitis, and stenosis).

4. Roentgenographically, peristaltic activity is readily seen in the right side of the colon, but dilated sigmoid shows little or no peristaltic activity or contraction.

These observations would seem to indicate that in a true megacolon there is some, yet unexplained, defect in innervation of the entire left side of the colon, whereas the right side of the large bowel retains normal activity. In support of this theory, anatomically at least, we know the parasympathetic innervation of the two sides of the colon to be different, i.e. the vagus supplies the right side of the colon, whereas the left side is supplied by the pelvic parasympathetic oneflow.

It must be emphasized that the operative procedure advocated is not merely a segmental colon resection. The removal of the dilated sigmoid alone has yielded unsatisfactory results. It must be clearly understood that the extent of resection is based on physiologic studies and entails the removal of 1. the narrowed rectosigmoid; 2. portions of the inactive colon, proximally to the right side of the transverse colon or ascending colon, where good peristaltic activity can be seen by roentgenogram.

The possible advantages of this procedure over the Swenson "pull-through" technic are:

1. This resection and anastomosis can be done entirely within the abdomen.

2. There is a possibility that the *nervi erigentes* may be damaged in the pull-through technic, because of the need for dissection and removal of a large portion of the rectum. Since this is a disease predominantly of males, this possibility must be given serious consideration.

Final evaluation of the "physiologic" colon resection described above must await several more decades. The initial results, however, have been most encouraging and have offered dramatic and gratifying results to the patient, parents, and to the surgeon.

Conclusions

1. Physiological studies of the colon, as determined by fluoroscopic and roentgenographic examinations after the administration of a barium enema in 18 patients with congenital megacolon reveal:

(a) a normal appearing rectum;

(b) a "narrowed" segment of the rectosigmoid and sigmoid portions of the colon of variable extent;

(c) marked dilatation and absence of peristaltic waves and normal haustral markings of the descending, sigmoid, and variable portions of the left side of the transverse colon;

(d) active peristalsis and normal haustral markings of the cecum, ascending, and right side of the transverse colon.

2. When the colon is exposed at laparotomy the differences between the right and left side of the colon are marked and correspond to the roentgenographic findings.

3. A one-stage transabdominal operative procedure is described in which the narrowed terminal segment of the sigmoid and portion of the colon showing no peristaltic activity roentgenographically are removed. The residual part of the large bowel (ascending and right side of the transverse colon) is then anastomosed to the upper portions of the rectum at a distance of 6 to 10 centimeters from the anal skin margin.

4. The operation described has been done in 18 patients without a death. Seventeen have had excellent results while the remaining patient has had to resort to enemas on several occasions since operation. The period of follow-up in these cases ranges from six to 48 months.

5. The saving of the rectum is of importance, because it eliminates the question of damage to the *nervi erigentes* which is a deterrent to the wholehearted acceptance of these operative procedures in which the rectum is removed.

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CLINICAL X-RAY STAFF CONFERENCES ON THE COLON*

V. Cancer of the Colon Found in a Patient Demonstrating Complete Duplication of Structures of Hind Gut Origin

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A 55-year old woman consulted us in June of 1948 complaining of blood in the stool and of intermittent, sharp, severe rectal pain. There had not been any abdominal pain or any weight loss. The patient has been told by her doctor several years previously that she had a partition in the rectum.

Fig. 1

Fig. 2

Fig. 1—Barium enema produced by intubation of the channel on the left side of the rectal septum. Note failure of rotation of the proximal colon and diverticulum of the transverse colon.

Fig. 2—Left colon, postevacuation film. Note diverticulum.

Examination of the rectum disclosed a thick, soft septum, sagittally placed and dividing the ampulla into two lumens, right and left, lined by normal rectal

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mucosa. This arrangement was symmetrical and consistent to the full length of the 25 cm. sigmoidoscope. There was normal bowel content in each lumen. Pelvic examination was noteworthy. The clitoris was normal but placed at the left of the mid-line. Symmetrically placed on the opposite side there was a healed scar which was a result of a surgical repair following a childhood skating accident. This scar apparently had been the site of a second clitoris. Posterior to the clitoris there were two orifices disposed side by side and each was proven, by catheterization, to be a urethral orifice.

The vagina was divided by a longitudinal septum into two openings, one very small, the other of normal size.

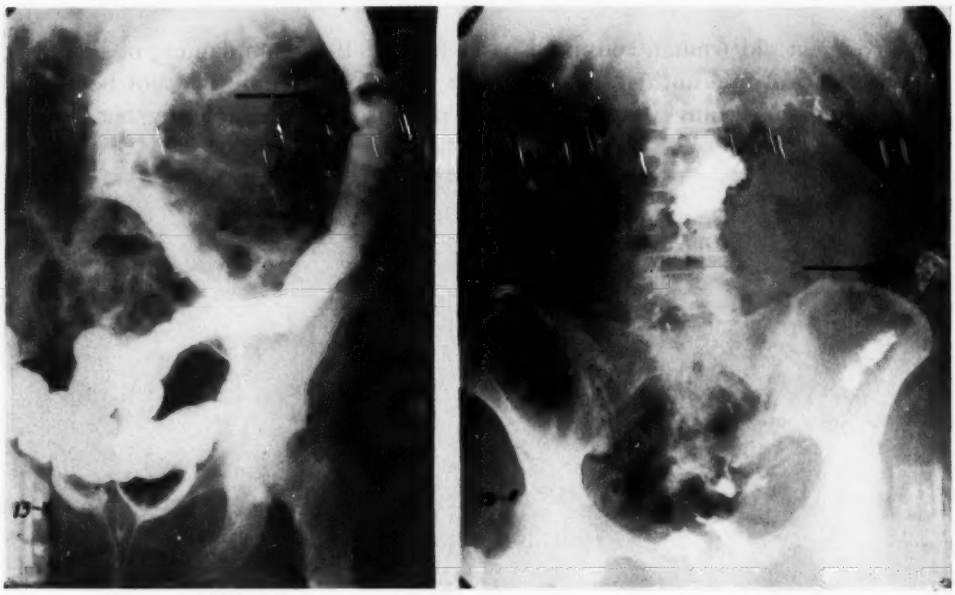

Fig. 3 Fig. 4

Fig. 3—Two retention balloons are present in the rectum, one on each side of the midline septum. Barium has been injected through the tube on the right side. Note failure of rotation of the proximal colon and large irregular polyp of the descending portion of the colon. This is obviously a different colon than the one demonstrated in Figs. 1 and 2.

Fig. 4—Right colon, postevacuation film. Note polyp.

The patient was severely hypertensive and was known to have had diabetes for several years. X-ray was recommended to search for the source of bleeding.

X-ray examination of this patient was begun by intubation of the left rectum. A colon of normal length was demonstrated, but showing failure of rotation of the right side of the colon (Fig. 1). (The cecum and ascending colon are contracted in this film). The terminal ileum extended into the right upper quadrant as in a typical nonrotation of the right side of the colon. A moderate size diverticulum was seen extending from the mid-portion of the

transverse colon. Postevacuation film (Fig. 2) demonstrated the distribution of the colon and terminal ileum to good advantage.

The next examination consisted of injection through a tube placed on the right side of the rectum (Fig. 3) (one tube was placed on each side to make certain of identification of the desired side). This demonstrated another identical colon, which exhibited the same failure of rotation of its right side. An irregular polyp was present in the descending portion of this colon. Postevacuation film also demonstrated the polyp (Fig. 4). In this film a small amount of barium is seen also in the left rectum and sigmoid, placed there for purposes of identification.

Fig. 5

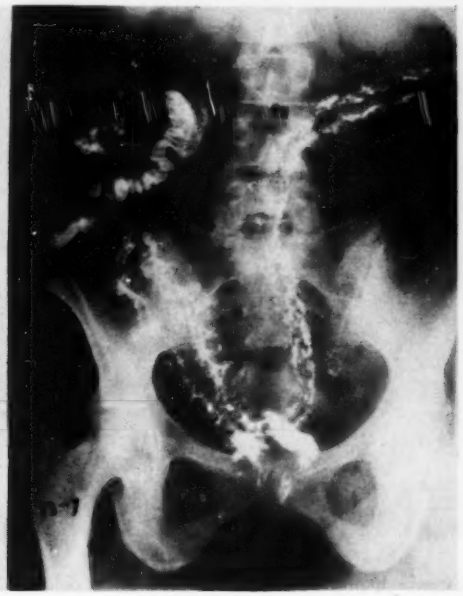

Fig. 6

Fig. 5—Barium has been injected on both sides of the rectal septum. The two colons follow a parallel, double-track arrangement. Note two ceca and two terminal ilea.

Fig. 6—Postevacuation film of both colons.

The next step of demonstration was to fill both colons simultaneously (Fig. 5). They followed a parallel, double track arrangement and two separate terminal ilia were present. Postevacuation film (Fig. 6) demonstrated the parallel arrangement nicely. In the double contrast film (Fig. 7) the polyp was clearly demonstrated. These films show that the patient possessed two parallel colons, each receiving a separate ileum and each showing failure of rotation. They were identical except for the presence of the diverticulum of the transverse portion of the left colon and the polyp in the descending portion of the right colon.

Because of the x-ray demonstration of the polypoid lesion in the descending colon, operation was done. Complete twinning of the terminal ileum and of the entire colon was found. This duplication started at a large Meckel's diverticulum and extended distally, there being two appendices and two complete colons attached exactly as the barrels of a shotgun are attached and each distinct from the other. A firm intraluminal lesion was palpated in the descending portion of the right colon. Colotomy was done and a firm, sessile polyp was found. The polyp was widely excised. Resection of the involved segment of bowel was not done, although indicated by the sessile nature of the polyp. Local excision

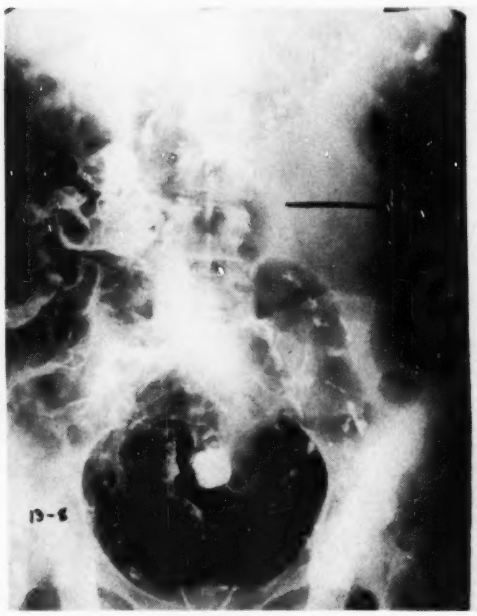

Fig. 7

Fig. 8

Fig. 7—Double contrast film of both colons. Note polyp.

Fig. 8—Recheck four years later. Return of rectal bleeding. Barium was injected into the right rectum (which previously contained a polyp). It progressed proximally to the mid-descending colon and then entered the left one of the two colons, spreading both proximally and distally. This is a fistula between the two colons, with complete retrograde obstruction of the right-sided one.

was chosen because of the severe hypertension of the patient and because of the additional operative trauma which would have been involved in the performance of a double segmental resection. The distribution of the blood supply made it impossible to resect a segment of one of the two colons without resecting the corresponding segment of its twin. Recovery of the patient from this procedure was uneventful.

The surgical specimen was a polyp 20 mm. long and 16 mm. in diameter which lacked a true pedicle, although a collar of normal appearing mucous membrane was attached to one pole. Histologically the lesion showed frank

carcinoma (Grade 1) with commencing invasion of the supporting stroma at the base of the lesion; a zone of normal tissue surrounded the deepest penetration of the tumor however, and it was felt at the time that a cure might have been obtained, although the prognosis was definitely guarded.

This patient did well for almost four years and then was readmitted to the hospital complaining of intermittent abdominal pain and fresh red rectal bleeding. X-ray studies were repeated.

A rectal tube was inserted on each side of the soft tissue rectal septum. A small amount of barium was injected first through one tube which was identified fluoroscopically as being in the left rectum. This injection was stopped after only

Fig. 9

Fig. 10

Fig. 9–Postevacuation film demonstrating the fistula between the twin colons.
Fig. 10–Double contrast demonstration of the obstruction and fistula.

a very small amount of barium had entered the left rectum, sufficient to identify it. The major injection was then carried out through the tube in the right rectum. It showed a normal appearance of the right colon up to the level of the mid-descending colon. A nearly complete obstruction was present at that point. The barium stopped, then eventually entered an irregular channel and appeared simultaneously in the distal loop of the left colon, running back down to the rectum, and in the proximal portion of the left colon, extending around to the cecum (Fig. 8). It was evident from the behavior of the barium during injection that a fistula existed between the twin colons in the mid-descending area at the point of nearly complete obstruction. The film demonstrated this

nicely and showed that the proximal colon which filled was the left colon, as proved by the demonstration of its diverticulum in the transverse area.

Postevacuation film (Fig. 9) showed a fairly good emptying of the *lower* segments of the left colon, although proximal to the point of obstruction it had emptied very little.

Air injection film (Fig. 10) also demonstrated the Y-shaped connection between the three filled portions of colon and the pooling of barium in the sinus tract between them.

It was concluded that a constricting lesion, presumably neoplastic involved both colons in the mid-descending area with a partial obstruction of the left colon and a complete obstruction of the right colon and with a fistula between the two parallel colons.

Fig. 11—Photograph during laparotomy demonstrating twin ceca and double appendices. The Meckel's diverticulum is held by the hemostat.

Laparotomy was done again. Our foreknowledge of the patient's developmental abnormality enabled us to prepare for and take several photographs at the operating table. The Meckel's diverticulum, the twin ceca and the double appendices with a fused tip are demonstrated photographically (Fig. 11).

An infiltrating, stenosing lesion was found at the site of the previous polypectomy. Resection of the involved loop was done. The technic of anastomosis was identical to that used in single-barreled anastomoses, each anastomosis having an inner row of continuous chromic cat-gut and an outer row of interrupted vertical mattress sutures of 000 black silk (Fig. 12). On the sixth postoperative day, at which time the patient was eating well and walking well and having good bowel movements, sudden unexpected death occurred. Autopsy was not granted.

The resected segment of colon (Fig. 13) was duplicated throughout its length, with complete fusion of about one-fourth of the circumference of either

barrel; each segment possessed three distinct taeniae, and when the common wall was sectioned longitudinally, two distinct muscle coats were easily seen. In the distal third of the specimen a typical neoplastic ulcer 3 cm. in diameter involved the fused portions of the gut segments and extended half way around the circumference of one barrel and about two-thirds of the circumference of the other, with some stenosis of the latter. Numerous nodules of metastatic tumor were found in the attached mesocolic fat, as far as 6 cm. from the primary; there was no enlargement of the nodes at the apex of the mesocolic wedge. Histologic examination revealed rather wide spread dissemination of adenocarcinoma throughout the adjacent mesocolic fat, with some involvement of lymph nodes as well; a block cut from the uninvolved common wall of the two colons showed partial fusion and interdigitation of the muscle coats and paucity of nerve elements.

Fig. 12–Ready for double-barreled anastomosis.

This case is of exceptional interest because it demonstrates an unusual anomaly and because it demonstrates the effect of that anomaly on the course of development of a carcinoma, with involvement of the nearby twin colon by direct extension of the carcinoma and development of a fistula between the two colons.

Reduplication of the colon or of a portion of the colon has been reported many times. Twenty-nine cases were collected in 1951. These 29 cases, however, fall into two distinct groups. Twenty-two of them consisted only of what was essentially a long diverticulum, arising from the colon and lying in the mesentery between the colon and the root of the mesentery and not accompanied by reduplication of other structures. These cases were found in the investigation of abdominal symptoms caused by the size of the abnormal structure, as a result of volvulus, or by ulceration and perforation of the abnormal structure. These 22 cases are considered to be diverticula derived from an already developed hind gut.

The other seven cases* found in the literature, including this case, differ in that in addition to the reduplication of colon they also show reduplication of the bladder and urethra. The anomaly in this smaller group of cases did not produce any symptoms except when there was imperforate anus or imperfect development of the partition between rectum and bladder. It is believed that this smaller group is caused by a true twinning of the hind gut at a stage when the embryonal tissue still retains its full developmental potentiality.

The hind gut of the embryo consists of that portion of the intestinal tube caudad to the yolk sac. The direction of growth of its anlage is caudad. At its caudal end it forms a cloaca which later is divided into a rectum posteriorly and a urogenital sinus anteriorly. This urogenital sinus later differentiates into the urethra, bladder, and urachus. It is obvious that any true twinning of the hind gut at a very early stage when its anlage still possesses its complete de-

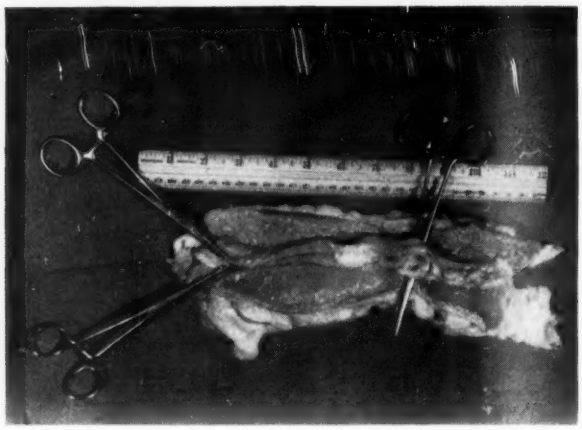

Fig. 13—Surgical specimen. Note the two parallel colons; the hemostat demonstrates the neoplastic fistula between the twin colons.

velopmental potentiality will result in duplication of all structures formed from it, including the bladder and urethra as in this case.

The difference between these two groups of cases is not one of origin of the anomaly since true twinning of the early anlage might conceivably take place at any point of its caudad growth. Rather it is a difference of time of origin of the extra cell masses, either early, when the cells still have the full developmental possibilities of hind gut anlage, or later when they are more differentiated and can produce only their own kind of structure. The statement that a true early twinning of the colon must be accompanied by twinning of the bladder and urethra is a paraphrase of a statement made by Volpé in 1900. He decided

*A similar case has recently been described by Mark M. Ravitch and William W. Scott, "Duplication of the entire colon, bladder and urethra", *Surgery*, **34**:843-858, (Nov.), 1953. In this case one of the two colons was incompletely developed distally, resulting in enormous distention of that colon.

from study of anomalies of the penis that the existence of a true double penis *presupposes* the existence of a double bladder and a double colon.

The hind gut does not give rise to the ureters, kidneys, vagina or uterus. In these seven cases of early twinning the kidneys and ureters have been normal but each ureter has emptied into a separate bladder, emptying through a separate urethra. The uterus and vagina have been double in all cases of the smaller group in the females even though these structures are not formed from the hind gut. This is a failure of fusion of the Mullerian ducts, perhaps because the urogenital sinus to which their distal ends attach is double in these cases and separated in space. This space separation may mechanically prevent the fusion which normally occurs in the structures derived from the two Mullerian ducts.

This is, therefore, one of seven cases which have been described as presenting reduplication of all the structures derived from the hind gut of the embryo.

DIARRHEAL SYNDROME*

Report on Therapy Using Resion with Polymyxin and Phthalylsulfacetamide

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"The etiology of diarrheas", according to Weiss[1], "is undoubtedly due to the abnormal irritation of the mucous membrane of the intestines by noxious substances, the prolonged use of certain drugs, or may be a symptom of general infectious diseases".

The introduction of antibiotics as therapeutic agents has created a syndrome referred to the gastrointestinal tract. Oral antibiotics in many patients produce disordered functions of the gastrointestinal tract, as manifested by a chain of physiologic disturbances capable of causing symptoms such as nausea, vomiting, severe abdominal cramps, frequency of bowel movements and distressing anal pruritus. We have been referring to this as the antibiotic diarrheal syndrome. The antibiotics have not only been deficient in producing bacteriologic cures in the intestinal tract, but are responsible for alterations in the intestinal flora permitting a strong overlay of yeast and mycotic infections. It has been demonstrated that various antibiotics can stimulate growth of bacteria *in vitro*[2], therefore, it is not beyond the realm of possibility that a direct stimulation of deleterious bacteria occurs in the course of at least certain of the antibiotics. The successful management of this syndrome poses a challenge to the physician and is becoming an increasingly serious problem.

The existing knowledge of the diarrheal syndrome is not too substantial, and as a result many cases are not properly diagnosed, thus leading to inadequate and often the wrong treatment. The physician must appreciate the significance of functional problems and know how to cope with them in order to obtain success in their management.

The objective of the physician in dealing with the diarrheal syndrome, irrespective of etiology, is to prescribe that treatment which will produce satisfactory relief of the distressing symptoms and control the diarrhea. The importance of the problem is exemplified in the many treatments available, and the need for a therapeutically efficient method continued to be obvious until the introduction of a multiple intestinal adsorbent, Resion.

Resion, consisting of polyamine anion exchange resin, synthetic sodium aluminum silicate, and synthetic magnesium aluminum silicate, was observed to have the capacity to inhibit lysozyme[3], to remove toxic amines[4], to adsorb

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bacterial metabolites[5], and to remove noxious agents comparable to shellfish poison[6]. Essential food factors, such as vitamins, minerals and amino acids, were not removed.

Clinically, Resion has been established as an effective treatment for diarrheas in pediatric practice[7,8], in the treatment of food poisoning[9], in the management of nausea and vomiting in pregnancy[10], and in the treatment of diarrheal syndrome associated with "virus enteritis", staphylococcus infection and dietary indiscretions[11,12].

Basically, Resion should be an ideal treatment for the usual cases of diarrhea; however, our problems were more profound. We were seeking a preparation with effective capacities in the management of 1) diarrheas following the use of oral antibiotics; 2) colitis diarrhea with ulceration; 3) irritable colon; and 4) summer infectious diarrhea.

Although Resion proved effective in a small percentage of the cases mentioned, this effectiveness was not consistent. The problem was presented to the research pharmacologists and in a short time an "improved" treatment was made available.

The Resion formula was fortified with Polymyxin and Phthalylsulfacetamide*. It was demonstrated that Polymyxin activity is not lost in the presence of Resion[13]. The oral administration of Polymyxin does not produce significant blood levels and has a rapid bacteriostatic action on most coliform bacteria and some cocci[14]. The Polymyxins are a group of polypeptides produced by B. polymyxin with high bactericidal activity against gram-negative bacteria. They are not significantly absorbed from the intestinal tract[15,16]. Polymyxin was found to be the ideal treatment of shigella infection in children[17].

Polymyxin B added to liquid cultures of candida albicans inhibited growth at concentrations as low as 250 units per milliliter, whereas this organism was stimulated by Neomycin at concentrations of 75 units or more per milliliter[18].

Phthalylsulfacetamide and Polymyxin showed a synergistic effect[13], and the combination seemed to be ideal for the treatment of infections related to the gastrointestinal tract. Sodium phthalylsulfacetamide is highly soluble at the physiological pH range of the intestinal tract. The oral administration of the drug is present as a highly concentrated solution in the contents of the small and large bowel. Although absorption into the blood stream from the lumen of the gut is minimal, considerable amounts diffused into the deeper strata of the intestinal wall. Findings indicate the compound possesses many desirable properties of an intestinal antiseptic[19].

Clinically, it has proven to be effective in reducing healing time in cases of surgery for hemorrhoids and other anorectal conditions. No postoperative infec-

*Supplied by the Medical Research Dept. of The National Drug Company, Philadelphia, Pa.

tions, allergic reactions nor any untoward effects were reported[20]. Restoration of normal stools, disappearance of pain, reduction of gas in intestines and return of x-ray and sigmoidoscopic findings to normal were reported[21] in 65 per cent of 28 patients with ulcerative colitis. It was suggested that the drug has a high potential of usefulness in this pathologic condition.

Resion plus Polymyxin and Phthalylsulfacetamide presented those features necessary for an ideal treatment of diarrheas representing serious medical problems. A study was set up to evaluate its effectiveness in 1) antibiotic diarrheal syndrome; 2) ulcerative colitis diarrhea; 3) summer diarrhea; 4) irritable colon.

Materials and Procedure

This study is made up of four groups of patients, representing different diarrhea syndromes. In every case an exhaustive clinical history was obtained, a thorough physical examination including a complete gastrointestinal series was made, and Resion with Polymyxin and Phthalylsulfacetamide was prescribed as an adjunct to treatment.

Group 1: Antibiotic diarrheal syndrome—12 patients:—In every patient in this group, the etiology of the diarrheal syndrome was definitely established as the ingestion of antibiotics for the treatment of some infections. The most significant complaints were severe lower abdominal cramps, nausea, vomiting, diarrhea and anal pruritus. This later symptom was present in 25 per cent of the patients, which was no doubt due to the presence of a marked overlay of yeast infection.

Our approach to this problem is presented in the two cases representative of the patients in this series:

Case 1:—B. F., Male, 38 years, white, waiter. No previous medical history. Came in because of a virus infection four weeks prior to the first visit. Had been treated with a full course of Terramycin, during which he developed diarrhea with cramps four to five times a day. Treated with paregoric and Kaopectate without benefit. Had lost eleven pounds in two weeks. Bowel movements were preceded by severe cramps, but no blood was ever noticed in the stool.

Laboratory findings:—Blood count showed Hb. 83 per cent, RBC 4,190,000, WBC 9,700, Polymorph. 74 per cent, lymph. 22 per cent and eos. 4 per cent. Urine was negative, including sugar and Indican.

Stool examination:—Appearance, brown and loose; reaction, acid; occult blood, positive; odor, foul; gas, large amount of mucus. Microscopically there were a few red cells and 80 per cent gram-negative bacilli.

Treatment:—This consisted of a low residue diet and Resion with Polymyxin and Phthalylsulfacetamide, one tablespoonful in water five times a day, which was reduced to four times a day after the second day. He showed a marked improvement immediately and in ten days we were able to discontinue the

Resion plus Polymyxin and Phthalylsulfacetamide. On October 13 another stool specimen was examined and showed quite an improvement. Occult blood was still positive. There was little if any gas and the amount of mucus had almost vanished. Microscopically no blood cells were seen and gram stain showed a 60 per cent positive, 40 per cent negative balance. Patient was seen again on November 7 and 21, 1952, and has not had any complaints since.

Case 2:—T. C., Male, age 38 years. Had been a patient for various complaints since 1934. Present illness began in December, 1952, following a tooth extraction for which he received penicillin and aureomycin. His complaints consisted of indigestion-like pains, distention and spasm of the rectum. He had noticed blood and pus in his bowel movement .

A barium enema showed a moderate descending colitis and questionable presence of polypi. Sigmoidoscopy revealed no ulcerations, although much mucus was present.

Treatment:—He was placed on Resion with Polymyxin and Phthalylsulfacetamide, one tablespoonful q.i.d.; by the second day he reported that his stools were large and formed, although soft. There was still some blood, but he did not have the indigestion pains or rectal cramps as before. In one week he was able to discontinue the treatment and subsequent stool examinations revealed a 55 per cent gram-positive distribution.

The remaining 10 cases in this group experienced the same gratifying relief from the abdominal cramps, distention, and where pruritus was a complaint this was relieved within an average of 72 hours. Diarrhea was controlled in an average of 48 hours, and in most cases it was possible to discontinue the medication within five days.

Group II: Ulcerative colitis diarrhea—10 patients:—We had tried plain Resion treatment in these patients without any therapeutic effect. This group was made up of patients between the ages of 22 and 65, equally divided between males and females. Most of them exhibited a strong psychic overlay which would make any medical approach difficult.

The concept that ulcerative colitis has a bacterial etiology[22,23], although not definitely proved, commended our consideration, and we decided to try the Resion with Polymyxin and Phthalylsulfacetamide as a therapeutic approach.

We believe a presentation of a few of the representative cases of this group will be of significance in showing the nature of the disease and our new therapeutic approach to this serious problem.

Case 3:—Mrs. F. H., 50-year old housewife, had been complaining of multiple watery bowel movements for the past 15 years. Movements varied from two to three a day to as many as 20 times a day, accompanied by cramps, diarrhea, bloating and mucus. Patient had been under a physician's care since

May, 1949 and had had several operations since that time for adhesions. The last operation, in December, 1952, consisted of an enterostomy for fibrosis of the pylorus. Patient persisted in her diarrhea symptoms and stool examination showed: appearance, brown and loose; reaction, acid; occult blood, positive; odor, foul; moderate amount of mucus.

Microscopically there were a few red blood cells, much undigested food, and yellow salts of calcium. The gram stain revealed 65 per cent gram-negative organisms.

In February, 1953 patient was started on one tablespoonful Resion with Polymyxin and Phthalylsulfacetamide q.i.d. with little results. One week later the medication was increased to two tablespoonfuls q.i.d. and the stools began to show some form. After three weeks on this medication there were two formed bowel movements daily, and subsequent stool examination revealed negative occult blood, no gas formation, reduction in the amount of mucus, no undigested food fibers, and the gram stain showed 55 per cent gram-positive.

Patient has been unstable since that time but each time her movements increase, two tablestpoonfuls of Resion with Polymyxin and Phthalylsulfacetamide are sufficient to check it.

Case 4:—Mr. M. H., 40-year old salesman, had been under a physician's care since May, 1946 because of colitis which was acquired while in the Armed Forces, for which he received treatment at Walter Reed General Hospital. In the beginning he would have as many as 40 bowel movements a day, all full of blood, gas and mucus, and accompanied by very strong abdominal pains. He had had varied forms of therapy and by 1949 was doing quite well, appearing about every six months for a check-up. In July of 1953 he suddenly began having multiple bloody bowel movements accompanied by abdominal and rectal pains. There was much pus noted in the movements.

A stool culture done June 14, 1953, showed many colonies of E. coli and Staph. albus. Barium enema done at that same time showed a marked ulcerative colitis of the descending colon with many polypi. Sigmoidoscopy revealed catarrhal inflammation of the mucosa, much adherent mucus, but no actual areas of bleeding could be determined.

Patient was placed on Chloromycetin, 250 mg. q. 6 h., and two tablespoonfuls of Resion with Polymyxin and Phthalylsulfacetamide q.i.d. By the third day these severe bowel movements had stopped, the cramps were less severe, the blood had almost completely vanished, and by the fifth day the patient was constipated. The Resion with Polymyxin and Phthalylsulfacetamide was reduced to one tablespoonful t.i.d., and the Chloromycetin was discontinued. On the tenth day sigmoidoscopy revealed a slightly hyperemic mucosa with minute capillary hemorrhagic areas. There was, however, no recurrence of the multiple bloody bowel movements.

Case 5:—Miss J. W., 22-year old dancer, is one of twins. Her sister is completely well. In June, 1951, she began having frequent multiple watery and bloody bowel movements accompanied by gas and nausea. She was hospitalized and after extensive work-up a diagnosis of ulcerative colitis was made. She was treated with 28 capsules of terramycin without any effect. She also received cortisone to the point where she developed hair on the face and forehead and fluid in the legs and abdomen. At one point her weight was down to 84 pounds. Her bowel movements continued to be loose and accompanied by blood despite all treatment. In April, 1953 and again in June, 1953 patient had additional blood transfusions. Stool culture failed to reveal any pathogenic organisms, and gram stain revealed 50 per cent positive, 50 per cent negative.

In April she was started on Resion with Polymyxin and Phthalylsulfacetamide, two tablespoonfuls q.4.h., without any results whatsover. This was discontinued after one month.

At present her weight is 113½, she feels better and has four movements a day, but it has been noted that when this patient gets a dancing part in some play or production there is always an improvement in her condition. She is presently happily at work.

Case 6:—Mr. H. B., 25-year old engineer, when first seen in 1951 had been subject to diarrhea, with four and more bowel movements daily for the past seven years. Four years previously he had received autovaccination with no results. From 1951 until March, 1953 he had received various forms of treatment, including Resion, Resinat, Dimethylane and other anti-diarrheal medication. In February, 1953 he had been having cramps in the stomach; eight and more watery, bloody bowel movements daily; and generally felt very uncomfortable. Barium enema in March, 1953 showed a pipestem descending colon with a complete loss of haustral markings.

Stool examination (one of many during the course of treatment) revealed: appearance, brown and mushy; reaction, acid; occult blood, positive; odor, foul; moderate amount of mucus; and microscopically, undigested food fibers. Gram stain showed 75 per cent gram-negative bacilli.

Patient was begun on one tablespoonful of Resion with Polymyxin and Phthalylsulfacetamide q.4 h., and in two weks stated that he felt pretty well. Bowels were formed and movements varied between one and two daily. No blood was noted. Abdomen felt soft and there were no cramps. The dose of Resion with Polymyxin and Phthalylsulfacetamide was reduced to one tablespoonful b.i.d. and discontinued two weeks later. Stool examination was repeated in June, 1953 and again in August, 1953. In each case it appeared practically normal, and the gram stain showed 50 per cent negative and 50 per cent positive.

The results in 9 out of the 10 patients were most gratifying. Diarrhea in a majority of the cases was controlled within five days, and in 50 per cent of the

cases the treatment was discontinued on the 10th day without recurrence of this symptom. In four patients, the diarrhea was adequately controlled with a maintenance dose of Resion with Polymyxin and Phthalylsulfacetamide. The youngest patient, a 22-year old female, failed to derive any benefit from the treatment.

Group III: Irritable colon—7 patients:—The history and physical examination definitely established the diagnosis in each of these patients as irritable colon. These did not present the therapeutic problem represented by the cases in groups I and II.

We prescribed Resion with Polymyxin and Phthalylsulfacetamide, one tablespoonful four times daily, and after the first day reduced the dose to one tablespoonful three times daily.

In four patients the results were more or less dramatic; the abdominal pain was completely relieved and the stools became firm within 36 hours. In five days all symptoms were absent; however, we continued therapy for an additional five days.

In three patients we added Homatropine Methylbromide, 2 mg. to each tablespoonful of the Resion-Polymyxin-Phthalylsulfacetamide, on the second day and continued this treatment for six days when all symptoms were absent. The Homatropine was discontinued at this time, but the treatment was continued with the Resion combination for an additional week with gratifying results in all cases.

Group IV: Summer diarrhea—25 patients:—These patients ranged in age from 18 to 65 years. This group represented the usual diarrheas encountered during hot summer months. The patients in most cases tried home and "drugstore" remedies for three to five days before seeking medical advice. A medical history did not reveal anything significant, except that they were having many bowel movements and could not get relief with certain remedies.

In all cases Resion with Polymyxin and Phthalylsulfacetamide, a tablespoonful at hourly intervals for three or four doses, then a tablespoonful every three hours, was prescribed.

Twelve of the patients reported relief within 24 hours; eight within 36 hours; two within 48 hours; and three did not continue with the treatment because of "taste" of the medication.

Summary

1. A new diarrhea syndrome designated antibiotic diarrhea syndrome is described.

2. A new treatment for various diarrheas is described. This contains a polyphasic intestinal adsorbent (Resion), Polymyxin and Phthalylsulfacetamide in a palatable vehicle.

3. Of the 12 patients in the antibiotic diarrhea group, all were relieved of cramps within 24 hours, and diarrhea controlled in an average of five days.

4. Of the 10 patients with ulcerative colitis diarrhea, 9 patients had gratifying results insofar as the control of diarrhea is concerned. A majority were brought under control within five days, and continued to be controlled as long as the medication was continued. One patient failed to derive any benefit.

5. Of the seven patients with irritable colon, four patients experienced dramatic relief; in three patients, the medication was fortified with Homatropine Methylbromide to achieve the desired results.

6. Of the 25 patients with summer diarrhea, 12 reported relief within 24 hours; 8 within 36 hours; and 2 within 48 hours. Three patients refused to continue with the medication because of its taste.

Conclusion

Our clinical experiences with Resion with Polymyxin and Phthalylsulfacetamide in the management of diarrheas of various etiologies lead us to believe that this treatment most nearly approaches the ideal for these diarrheal syndromes.

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FAVORABLE CLINICAL RESULTS IN CARDIOSPASM WITH ANTICHOLINERGIC MEDICATION (OXYPHENOMIUM BROMIDE)

Preliminary Report

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and

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Cardiospasm has been subjected to intensive study in recent years. The symptomatology and diagnosis of this disturbance are well established[1]. Medical management is the method of choice and surgery resorted to much less frequently. Medical treatment, however, has often been unsatisfactory. The primary mode of therapy in almost all cases of cardiospasm has been hydrostatic dilatation of the esophagogastric junction. Recently Balfour and Wharton[2] have reported excellent results with orally administered procaine, and Nickerson and Call[3] obtained relaxation of the cardia for three or four days after intravenous injection of dibenamine.

Recentiy, we undertook a clinical experiment to evaluate the possible effect of an anticholinergic medication, oxyphenonium bromide*, in cardiospasm. Six patients with this disorder were administered 5 mg. of oxyphenonium bromide, 30 to 45 minutes before meals and before retiring. One patient with marked esophageal stasis and retention had preliminary nightly aspirations and lavage. Three of the patients had short courses of hydrostatic dilatation at the onset of treatment. There has been marked symptomatic improvement in the entire group of patients. They are being maintained for an indefinite period on the above dosage pending further study and clinical evaluation. They are maintained on a bland, low residue, soft diet and were advised to avoid very hot or cold foods and beverages. Phenobarbital was prescribed to allay tension when required.

The rationale for the use of potent anticholinergic drugs in the medical management of cardiospasm has not yet been definitely established. The fundamental studies of Kramer and Ingelfinger[4], as well as Butin and associates[5] on the basic motility pattern of the esophagus in cardiospasm and its sensitivity to methylcholine chloride (mecholyl), however, may furnish at least a partial explanation. Their findings indicate that cardiospasm is primarily a neuromuscular disorder which involves not only the cardia but the lower two-thirds of the esophagus. Patients with cardiospasm exhibited a tetanic-like contracttion of the esophagus with substernal pain and an increase in the intraesophageal

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From the Division of Gastroenterology, Department of Medicine, Jewish Hospital of Brooklyn.

*Antrenyl (Ciba).

pressure to an average of 60 cm. of water following subcutaneous injection of 6 to 10 mg. of mecholyl. Normal persons and those with obstructing carcinoma, stricture, localized spasm or scleroderma, exhibited very little or no reaction. Rowen and coworkers[6] demonstrated an inhibitory effect by oxyphenonium bromide on esophageal motility after mecholyl motor stimulation in a patient with cardiospasm.

The clinical results with oxyphenonium bromide in this group of six patients has been most encouraging in the treatment of this perplexing and disturbing disorder. Roentgen studies are in progress to evaluate the effect of oxyphenonium bromide on the esophagus emptying time. This medication should not be considered the sole form of therapy in cardiospasm. It is employed as an adjuvant to customary medical management including occasional hydrostatic dilatation. Further investigations and evaluation of this therapy by others would be desirable.

Summary

1. Anticholinergic medication (oxyphenonium bromide) has proved effectual in a group of patients with cardiospasm.

2. An increased sensitivity of the esophagus to drugs such as methylcholine chloride (mecholyl) has recently been demonstrated by several investigators. This suggests a possible explanation for the efficacy of anticholinergic drugs as adjuvants in the management and treatment of cardiospasm.

Addendum

Since submitting this paper we found it necessary to increase the dosage of oxyphenonium bromide (Antrenyl–Ciba) to 10 mg. four times daily. The dosage may be varied according to the clinical requirements.

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President's Message

The American College of Gastroenterology has begun its official existence. At the special meeting of Fellows of the National Gastroenterological Association held in New York, 2 May 1954, the final steps were taken and now development must begin.

One of the first projects to be undertaken by the College will be to develop a research program.

At the regional meeting held in Milwaukee, Dr. H. Necheles, chairman of the research committee, gave the Board of Trustees a thrilling preview of a research program which is to be lanuched at our annual convention in Washington, D. C. in October.

As a result of this presentation and discussion of the research committee, individual members of the Board of Trustees voluntarily subscribed to an initial research fund to get the program started.

Dr. Lynn A. Ferguson and his Program Committee have completed the convention program which is one of the best we have ever had.

Dr. William W. Lermann and his Postgraduate Education Committee have completed the program for our postgraduate course, and this is also one of the best we have ever had.

The Executive Committee was authorized by the Board of Trustees to propose a Board of Governors for the College, and this work is well under way.

The spirit of cooperation which has been manifest at all meetings, has been an inspiration to your president. I wish to express my thanks and appreciation to all the trustees, Fellows, committee members and others who have had a part in organizing the College. There has been a complete unanimity of purpose and this augurs well for the future.

Sigurd W. Johnsen

EDITORIAL

Primary Tumor of the Retroperitoneum

It is rather difficult to make an early diagnosis of retroperitoneal tumor as the symptoms are inadequate and the tumor can grow to a very large size before actual manifestations appear or are recognized. Even after recognition of the mass, operation may be late.

Among the symptoms that the patient may experience or complain of are a vague feeling of abdominal fullness or discomfort as the tumor grows and the abdomen becomes distended or enlarged. Some patients become nauseous, vomit, have cramps, diarrhea, constipation, or develop large hemorrhoids. Later ascites, dyspnea, hematemesis, bloody stools, or partial or complete obstruction of the bowel may occur.

The patient speaks of uneasiness or vague pain in the back radiating down one or both extremities due to pressure or involvement of the lumbar and/or the sacral nerves. Edema, changes in surface temperature and varicosities, involving one or both limbs, appear because of retroperitoneal blood vessels and lymphatic changes which take place due to pressure of the tumor.

In addition to the above symptoms, the kidney, ureter and the spleen may be displaced and add to the difficulty of diagnosis. Dysuria, hematuria urgency and, in the later stages, anuria may be present due to pressure of the retroperitoneal tumor against the bladder.

When the spleen is displaced anteriorly by the tumor, differential diagnosis will be rather difficult because of left-sided retroperitoneal tumor may mimic a duodenal ulcer, colitis, tumor or diverticulitis of the large intestine, while a retroperitoneal mass on the right-side may point towards biliary or cholecystic involvement.

Physical examination reveals a painless abdominal mass which varies in size, mobility and ballottement. Some of the larger tumors are benign, while smaller tumors may be malignant. Therefore, the size of the mass is not an important factor, rather, fixation of the tumor is of great import. Fixation of the mass is usually associated with malignant tumors, while mobility and ballottement speak for nonmalignant growths.

X-ray examination of the abdominal organs may show displacement of the stomach, forward, upward or transversely. The duodenum, small intestine and colon may also show pressure or displacement when a retroperitoneal tumor is present. It may also cause distortion of the kidney and ureter which is readily recognized by a simultaneous presacral retroperitoneal pneumogram and retrograde pyelogram.

Samuel Weiss, M.D.

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In Memoriam

We record with profound sorrow the passing of Dr. James C. Droste, Grand Rapids, Mich., Associate Fellow of the National Gastroenterological Association.

We extend our deepest sympathy to the bereaved family.

ABSTRACTS FOR GASTROENTEROLOGISTS

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STOMACH

JEJUNOGASTRIC INTUSSUSCEPTION: C. P. Wisoff, Radiology. 61:363-367 (Sept.), 1953.

Two cases of jejunogastric intussusception following gastroenterostomy are presented, adding to the more than 100 which have already appeared in the literature. Four types have been encountered: (1) intussusception of the efferent loop of the gastrojejunostomy are most common, (2) of the afferent loop, (3) of both loops, and (4) intussusception following subtotal gastrectomy. Symtoms and signs are either of the acute or chronic type, depending on the degree and reducibility of the obstruction. A mistaken diagnosis of mechanical obstruction or bleeding ulcer is usually made, but the roentgen findings are pathognomonic. There is a circumscribed intraluminal defect in the stomach, the outer surface of which shows the concentric striations of *valvulae conniventes*, in a patient who has had a gastroenterostomy. Surgical treatment usually relieves the symptoms and may be lifesaving in the acute cases.

ARNOLD L. BERGER

PYLORIC ANTRAL MUCOSAL DIAPHRAGM: K. E. Gross and M. W. Durham, Radiology, 61:368-371 (Sept.), 1953.

A case of partial obstruction in the stomach is reported in which there occurred a hymen-like ring of mucosa, muscularis mucosa and submucosa. Symptoms were intermittent vomiting of several years' duration, aggravated by solid food and partially relieved by a liquid diet, and a sensation of fulness in the upper abdomen, but no pain. Surgical intervention was followed by postoperative improvement. The hymen-like diaphragm is believed to be of congenital origin. Only one other case was found in a review of the literature.

ARNOLD L. BERGER

SITUS INVERSUS OF STOMACH: F. H. VOLK, and C. M. Graney, Radiology, 61: 376-378 (Sept.), 1953.

A case of an extremely rare type of partial situs inversus is presented. The stomach lay to the side and posterior to the right lobe of the liver, which was in normal position, together with the gallbladder. The diaphragm was normal, as differentiated from the majority of cases of right-sided stomach, which are associated with eventration of the diaphragm. The existence of the anomaly was discovered during cholecystectomy and later confirmed by roentgenologic studies.

ARNOLD L. BERGER

BOOK REVIEWS FOR GASTROENTEROLOGISTS

HUMAN EMBRYOLOGY: Bradley M. Patten, Professor of Anatomy, University of Michigan Medical School. Second Edition. 798 pages, illustrated—some in colors. The Blakiston Company, Inc., New York, N. Y., 1953. Price $12.00.

Although the study of histology by many medical students is considered as a non-essential branch of the medical curriculum, nontheless it is an important subject as it is the introduction to pathology. Recognition of normal tissue aids the student in further enhancement of his knowledge in recognizing which is abnormal and which is pathological.

Dr. Patten's book is easily read and assimilated by the student because it is clear, concise and well illustrated.

Not only the medical student but the busy physician is urged to read carefully the interesting chapters dealing with the development of the human embryo, twins, monsters, etc.

The author and the publisher deserve credit for the publication of this timely volume.

DIABETES MELLITUS (Die Zuckerkrankheit) for students and practitioners, by Prof. Dr. E. Bertram. 4th revised edition. 175 pages, 25 illustrations and 9 tables. Georg Thieme Verlag, Stuttgart, 1953. Price DM 19.80.

A well written documentary small volume dealing with diabetes and its modern treatment. The various types of insulin, their indications, reactions, etc., are discussed fully. Attention is called to allergic reactions, edema, dangers, lipodystrophy, etc. of insulin. Diabetic coma and its treatment is a worthwhile part of the book. In fact, it is rather a unique presentation of an interesting subject in compact form.

ZUR GENESE DES DIABETES MELLITUS UND DES BRONCHIALASTHMAS by Prof. Dr. M. Bauer with a foreword by Dr. Cl. Dierkes. 113 pages, 5 illustrations. Georg Thieme Verlag, Stuttgart, 1953. Price DM 9.60.

One of a series of monographs dealing with the causes of diabetes mellitus and asthma. It is interesting but tedious reading, especially for those physicians who do not read the German language fluently.

Translation into English would enhance the brochure's value.

TRANSACTIONS OF THE FOURTH MEETING OF THE INTERNATIONAL SOCIETY OF GEOGRAPHICAL PATHOLOGY—Liege, 15-18 July 1952: 652 pages, illustrated. S. Karger, Basel, 1953.

This volume contains the numerous papers read at the International Society of Geographical Pathology and deals with many phases of diagnosis of affections of the liver and nutrition as found in various geographic areas in America and Europe.

Health officers, bacteriologists and pathologists will find it useful in their daily routine.

DISEASES OF THE CHEST: T. Royle Dawber, M.D., F.A.C.P. and Lloyd E. Hawes, M.D., D.A.B.R. 440 pages, well illustrated. The Williams and Wilkins Company, Baltimore, Md., 1953. Price $10.00.

This is a well written book with beautiful and clear illustrations and explanatory text, printed on heavy stock in readable type. Neither the authors nor the publishers skimped in the make-up of this valuable addition to the physician's library.

Medical students as well as physicians will find this volume dealing with diseases of the chest an unusual and clear text with useful information. It is highly recommended.

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*Steigmann, F., and Goldberg, E., J. Lab. & Clin. Med. *42*:955 (1953).

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the FLEET ENEMA

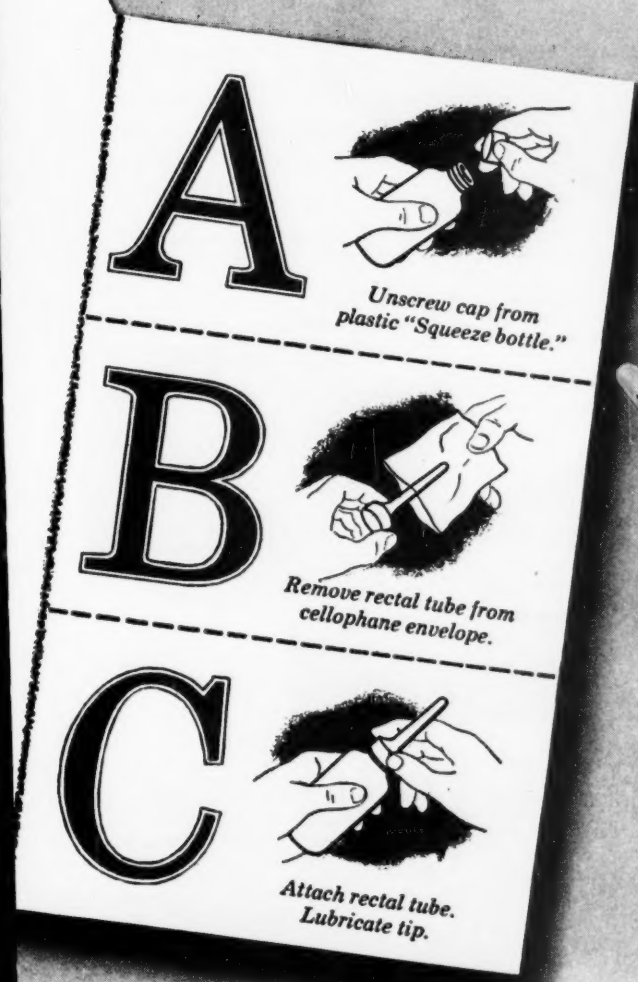
Disposable Unit

Polyethylene "squeeze bottle" permits easy one-hand administration... rectal tube kept sanitary by sealed cellophane envelope... distinctive rubber diaphragm prevents leakage while controlling flow. Because of these unique features, FLEET ENEMA Disposable Unit is preferred for hospital, clinic and office use.

Each single use unit of 4½ fl. ozs., contains in each 100 cc., 16 Gm. sodium biphosphate and 6 Gm. sodium phosphate,... an enema solution of Phospho-Soda (Fleet), gentle, prompt, thorough—and as effective as the average enema of one or two pints.

C. B. FLEET CO., INC.
Lynchburg • Virginia

'Phospho-Soda' and 'Fleet' are registered trademarks of C. B. Fleet Co., Inc.



first flight

Without trust in Daddy's strong arms, fear would blot out the fun of first flight. But because Daddy's smiling, loving face is below, life adds a thrilling new dimension, founded in love and trust.

All our adventures begin in and come home to the security we cannot do without.

To give and to get security is the main business of living. It is a privilege and a responsibility. It provides us life's finest rewards.

Have you ever thought that this security is possible only in a democracy? We continue to grow stronger as a nation when more and more secure homes are bulwarked together. The security of your country depends on *your* security.

Saving for security is easy! Here's a savings system that really works—the Payroll Savings Plan for investing in United States Savings Bonds.

This is all you do. Go to your company's pay office, choose the amount you want to save—a couple of dollars a payday, or as much as you wish. That money will be set aside for you before you even draw your pay. And automatically invested in United States Series "E" Savings Bonds which are turned over to you.

If you can save only $3.75 a week on the Plan, in 9 years and 8 months you will have $2,137.30.

U. S. Series "E" Savings Bonds earn interest at an average of 3% per year, compounded semi-annually, when held to maturity! And they can go on earning interest for as long as 19 years and 8 months if you wish, giving you back 80% more than you put in!

For your sake, and your family's, too, how about signing up today?

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Effectiveness + Convenience

IN THE MANAGEMENT OF CONSTIPATION

In the management of constipation bland bulk helps to reestablish normal elimination. Mucilose represents an especially well suited product because it is of vegetable origin and absorbs 50 times its own weight of water, forming a bland, non-absorbable, non-digestible, soothing gel.

With Mucilose there is the added convenience and ease of adjusting the dosage form to meet the clinical need of the patient.

1 **Mucilose Granules Special Formula (with dextrose),** tins of 4 oz. and 1 lb. Pleasant tasting, crunchy granules.

2 **Mucilose Flakes Special Formula (with dextrose),** tins of 4 oz. and 1 lb. Pleasant tasting, easily dispersed in water or other liquids.

3 **Mucilose Flakes Concentrated,** tins of 4 oz. and 1 lb. Sugar free (non-caloric), especially useful for the management of constipation in the diabetic and obese patient.

4 **Mucilose Compound Tablets,** bottles of 100 and 1000. Mucilose with methylcellulose. Easy to swallow, convenient to carry.

5 **Mucilose with Cascara Granules,** tins of 4 oz. Contain 1 grain of powdered cascara per heaping teaspoonful (5 Gm.). Particularly valuable during transitional treatment of the confirmed user of strong laxatives.

Mucilose should be taken with 1 or 2 glasses of water.

Mucilose®

BLAND BULK HYDROGEL

For Physiologic Bowel Regulation

WINTHROP-STEARNS INC. NEW YORK 18, N. Y. • WINDSOR, ONT.

Mucilose, trademark reg. U. S. & Canada

TREVIDAL®

the Ideal Antacid for the Treatment of Hyperacidity, Gastritis, and Peptic Ulcer

Fast Action

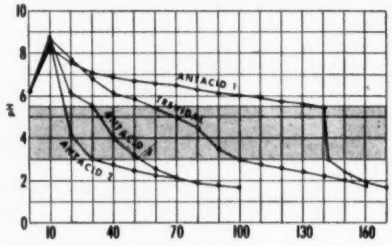
Trevidal tablets provide fast relief for they disintegrate completely in less than a minute.

Protective Coating

Regonol, a unique vegetable gum, assures a mucilaginous protective coating to irritated stomach surfaces.

Prolonged Effect

Egraine, a special binder from oat flour, plus a balanced formula of antacids assures prolonged antacid activity.



BALANCED FORMULA

aluminum hydroxide gel, dried	90 mg.
calcium carbonate	105 mg.
magnesium trisilicate	150 mg.
magnesium carbonate	60 mg.
Egraine*	45 mg.
Regonol*†	100 mg.

In each tablet, this balance of slow- and fast-acting antacids designed to avoid constipation, diarrhea, and alkalosis.

Prescribe Trevidal in boxes of 100 tablets, specially stripped for easier carrying.

*Trade Mark †Cyamopsis tetragonoloba gum

Organon INC. • ORANGE, N. J.

"complete symptomatic relief"[1] *in peptic ulcer patients...*

Antrenyl®

In a recent study, patients with acute symptoms of peptic ulcer obtained relief 24 to 36 hours after taking Antrenyl, a potent anti-ulcer agent.

ANTRENYL—prescribed as an adjunct to rest, sedation, antacids and diet—offers the peptic ulcer patient optimal benefits. It is also of value in other conditions marked by gastrointestinal spasm.

ANTRENYL inhibits gastrointestinal motility and gastric secretion. Side effects are either mild or absent, and there is no bitter aftertaste.

ANTRENYL is available as tablets (white, scored), 5 mg.; syrup, 5 mg. per 4-ml. teaspoonful; tablets (peach-colored, scored), 5 mg. with phenobarbital, 15 mg.; Pediatric Drops (with dropper), each drop containing 1 mg. of Antrenyl bromide.

1. ROGERS, M.P., AND GRAY, G.L.: AM. J. DIGEST. DIS. 19:180 (JUNE) 1952.

Antrenyl® bromide (oxyphenonium bromide CIBA)

CIBA
SUMMIT, N. J.

c/20324

large gastric ulcer

Fig. 3, Case 103 before therapy.

healed with

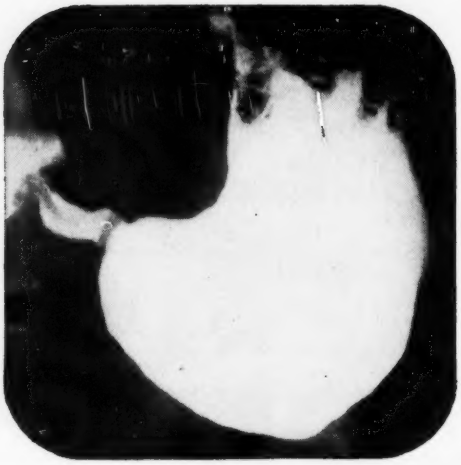


Fig. 6, Case 103 after 4 months PRANTAL therapy.
* Heineken, T. S.: Rev. Gastroenterol. **20**:829, 1953.

PRANTAL...*relieves pain*

*facilitates healing • "least side actions"**

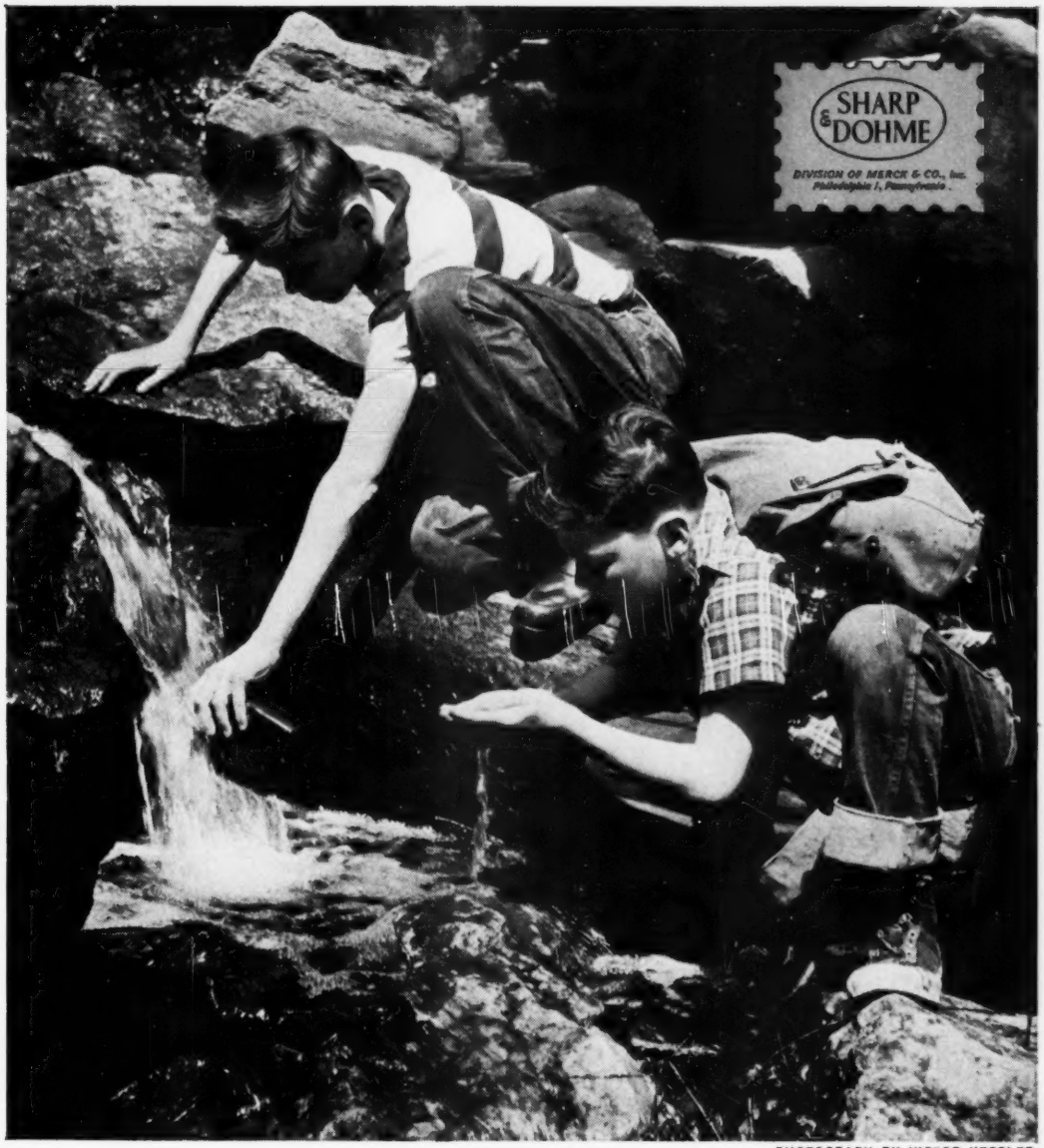
widest variety of dosage forms

PRANTAL® Methylsulfate, brand of diphenmethanil methylsulfate.

Schering

PRANTAL

SCHERING



PHOTOGRAPH BY VICTOR KEPPLER

When diarrhea attacks the unwary...

CREMOSUXIDINE®

SULFASUXIDINE® SUSPENSION WITH PECTIN AND KAOLIN

The hazards of contaminated water and food are often carelessly overlooked by your patients on a holiday.

You can quickly and safely check specific and non-specific diarrheas with CREMOSUXIDINE. This tasty, chocolate-mint suspension contains three therapeutic agents...'Sulfasuxidine' which provides a "most satisfactory intestinal antiseptic,"[1] plus pectin and kaolin, which inactivate toxins and soothe inflamed mucosa.

Quick Information: *Adult dosage:* 1½ to 2 tablespoonfuls six times a day. *Children* and *infants* in proportion.

Reference: 1. J. A. M. A. 153:1519 (Dec. 26) 1953.

"... the gastric secretion is the immediate agent of mucosal tissue digestion.... Opposed to this stands the defensive factor ... the two-component mucous barrier"[1] *[the protecting layer of mucus and the mucosal epithelium].*

Rotational gastroscopic views showing coating effect 1½ hours after administration of Amphojel.[2]

Causation — key to treatment in peptic ulcer

Through *topical* action alone, AMPHOJEL contends with the local causes of ulcer—aggressive acidity coupled with impairment of the wall defenses. Providing a dual approach, AMPHOJEL combines two aluminum hydroxide gels, one reactive, one demulcent. The reactive gel combats the attacking factor in ulcer by promptly buffering gastric acid. The demulcent gel promotes healing of the denuded mucosa by forming a viscous, protective coagulum.

AMPHOJEL—nonsystemic, nontoxic—provides time-proved *fundamental* therapy.

AMPHOJEL®

ALUMINUM HYDROXIDE GEL

Supplied: Liquid, bottles of 12 fluidounces
Tablets, 5 grain, boxes of 30, bottles of 100;
and 10 grain, boxes of 60 and 1000

References: 1. Hollander, F.: Arch. Int. Med. 93:107 (Jan.) 1954
2. Deutsch, E.: Scientific Exhibit, Gastroscopy, Interim Session A.M.A., St. Louis, December, 1953

Wyeth®
Philadelphia 2, Pa.